ANTHROPOMETRIC MEASUREMENTS AND CENTRAL OBESITY – A MAJOR PREDICTOR OF CARDIOVASCULAR DISEASE RISK IN WOMEN- A CROSS SECTIONAL STUDY

Dissertation submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY
CHENNAI – 600 032

In partial fulfilment of the requirement for the degree of
Doctor of Medicine in Physiology (Branch V)

M.D. (PHYSIOLOGY)
MAY – 2018

DEPARTMENT OF PHYSIOLOGY
TIRUNELVELI MEDICAL COLLEGE
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CERTIFICATE

This is to certify that the dissertation entitled, **"ANTHROPOMETRIC MEASUREMENTS AND CENTRAL OBESITY – A MAJOR PREDICTOR OF CARDIOVASCULAR DISEASE RISK IN WOMEN- A CROSS SECTIONAL STUDY"** done by Dr. G.SHERRY JENILIN post graduate in PHYSIOLOGY (2015-2018), is a bonafide research work carried out under our direct supervision and guidance and is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, for M.D. Degree Examination in Physiology (Branch V), to be held in May 2018.

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ENDORSEMENT BY THE GUIDE

This is to certify that the dissertation entitled, **"ANTHROPOMETRIC MEASUREMENTS AND CENTRAL OBESITY – A MAJOR PREDICTOR OF CARDIOVASCULAR DISEASE RISK IN WOMEN- A CROSS SECTIONAL STUDY''** is a bonafide research work carried out by Dr. G.SHERRY JENILIN, in the Department of Physiology, Tirunelveli Medical College Hospital, Tirunelveli – 11 under my direct guidance and supervision in partial fulfilment of the requirement for the award of the degree of MD in PHYSIOLOGY (Branch – V) in May 2018.

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DECLARATION

I solemnly declare that the dissertation entitled **"ANTHROPOMETRIC MEASUREMENTS AND CENTRAL OBESITY – A MAJOR PREDICTOR OF CARDIOVASCULAR DISEASE RISK IN WOMEN- A CROSS SECTIONAL STUDY''** is done by me at Tirunelveli Medical College Hospital, Tirunelveli.

The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfilment of the requirement for the award of M.D. Degree (Branch V) in Physiology.

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PROTOCOL TITLE: ANTHROPOMETRIC MEASUREMENTS AND CENTRAL OBESITY – A MAJOR PREDICTOR OF CARDIOVASCULAR DISEASE RISK IN WOMEN –CROSS-SECTIONAL STUDY

PRINCIPAL INVESTIGATOR: DR.G.SHERRY JENILIN, MBBS.,

DESIGNATION OF PRINCIPAL INVESTIGATOR POST GRADUATE I YEAR IN PHYSIOLOGY
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE , TIRUNELVELI

Dear , Dr.G.Sherry Jenilin, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.12.15.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1. TIREC Application Form ☐
2. Study Protocol ☐
3. Department Research Committee Approval ☐
4. Patient Information Document and Consent Form in English and Vernacular Language ☐
5. Investigator's Brochure ☐
6. Proposed Methods for Patient Accrual Proposed ☐
7. Curriculum Vitae of the Principal Investigator ☐
8. Insurance /Compensation Policy ☐
9. Investigator's Agreement with Sponsor ☐
10. Investigator's Undertaking ☐
11. DCGI/DGFT approval ☐
12. Clinical Trial Agreement (CTA) ☐
13. Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA) ☐
14. Clinical Trials Registry-India (CTRI) Registration ☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
   e. Approval for amendment changes must be obtained prior to implementation of changes.
   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in the protocol must be informed.

STANDS APPROVED UNDER SEAL

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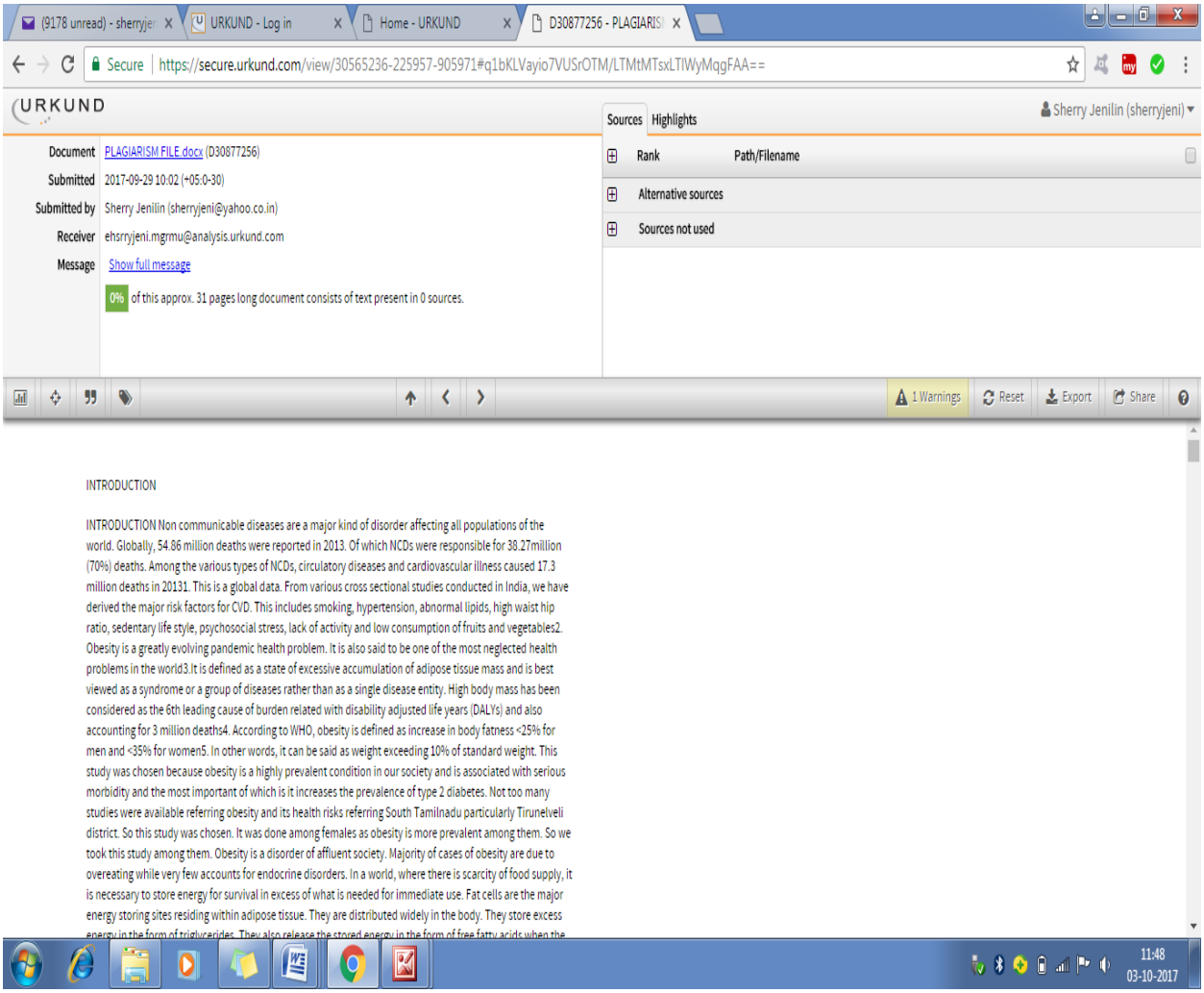
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INTRODUCTION
INTRODUCTION Non communicable diseases are a major kind of disorder affecting all populations of the world. Globally, 54.86 million deaths were reported in 2013. Of which NCDs were responsible for 38.27million (70%) deaths. Among the various types of NCDs, circulatory diseases and cardiovascular illness caused 17.3 million deaths in 20131. This is a global data. From various cross sectional studies conducted in India, we have derived the major risk factors for CVD. This includes smoking, hypertension, abnormal lipids, high waist hip ratio, sedentary life style, psychosocial stress, lack of activity and low consumption of fruits and vegetables2. Obesity is a greatly evolving pandemic health problem. It is also said to be one of the most neglected health problems in the world3.It is defined as a state of excessive accumulation of adipose tissue mass and is best viewed as a syndrome or a group of diseases rather than as a single disease entity. High body mass has been considered as the 6th leading cause of burden related with disability adjusted life years (DALYs) and also accounting for 3 million deaths4. According to WHO, obesity is defined as increase in body fatness <25% for men and <35% for women5. In other words, it can be said as weight exceeding 10% of standard weight. This study was chosen because obesity is a highly prevalent condition in our society and is associated with serious morbidity and the most important of which is it increases the prevalence of type 2 diabetes. Not too many studies were available referring obesity and its health risks referring South Tamilnadu particularly Tirunelveli district. So this study was chosen. It was done among females as obesity is more prevalent among them. So we took this study among them. Obesity is a disorder of affluent society. Majority of cases of obesity are due to overeating while very few accounts for endocrine disorders. In a world, where there is scarcity of food supply, it is necessary to store energy for survival in excess of what is needed for immediate use. Fat cells are the major energy storing sites residing within adipose tissue. They are distributed widely in the body. They store excess energy in the form of triglycerides. They also release the stored energy in the form of free fatty acids when the
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03-10-2017

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled **Anthropometric measurements and central obesity- A major predictor of cardiovascular disease risk in women- A Cross sectional study** of the candidate **Dr.G.SHERRY JENILIN** with registration Number **201515302** for the award of **MD Degree** in the branch of **PHYSIOLOGY(Branch-V)**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **0%** percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

ACKNOWLEDGEMENT

First, I thank my **God, the Almighty** for providing me this opportunity to do a study and complete it successfully.

- I sincerely express my heartful gratitude to our beloved **Dean, Prof. Dr. K. Sithy Athiya Munavarah M.D.** and to our respected **Vice Principal Prof. Dr.C.Revathy M.D.,** Tirunelveli Medical College, Tirunelveli for their encouragement during the study period.
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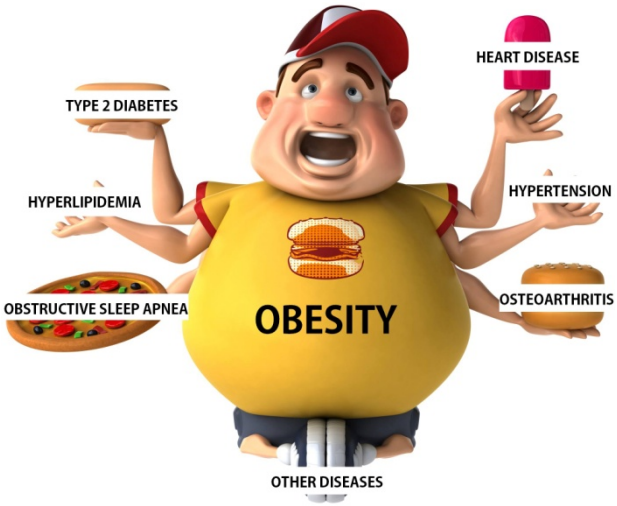
- Last, but **an important note of thanks to all participants of this study** without whom this could not be accomplished.
- Above all, a heartful thanks to **my mom, dad , husband and kid** who had given the space I need to complete this study.

CONTENTS

LIST OF ABBREVIATIONS

NCD	Non Communicable diseases
WHO	World Health Organization
CVD	Cardio Vascular Diseases
BMI	Body Mass Index
WC	Waist Circumference
WHR	Waist Hip Ratio
SFT	Skin Fold Thickness
DM	Diabetes Mellitus
TGL	Triglyceride
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
SAAT	Subcutaneous abdominal adipose tissue
IAAT	Intra-abdominal adipose tissue
TEF	Thermic Effect of Food
REE	Resting Energy Expenditure

TEE	Total daily Energy Expenditure
FFA	Free Fatty Acid
LPL	Lipo Protein Lipase
TOFI	Thin on the Inside Fat on the Outside
VAT	Visceral Adipose Tissue



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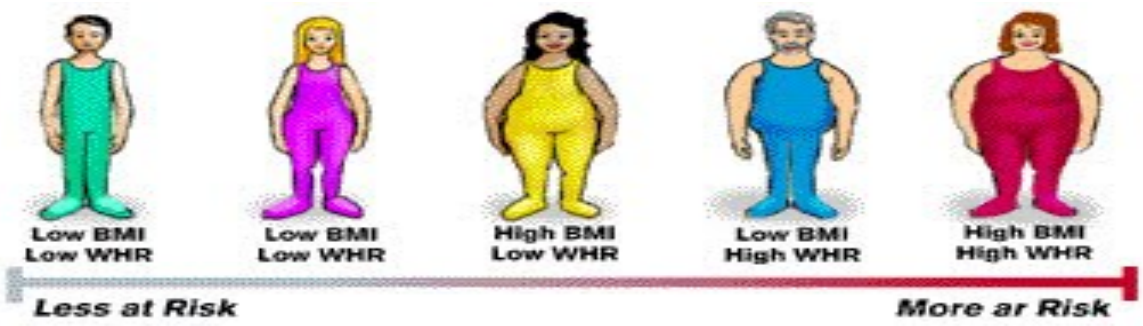

INTRODUCTION

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Non communicable diseases are a major kind of disorder affecting all populations of the world. Globally, 54.86 million deaths were reported in 2013. Of which NCDs were responsible for 38.27million (70%) deaths. Among the various types of NCDs, circulatory diseases and cardiovascular illness caused 17.3 million deaths in 2013[1]. This is a global data. Many cross sectional studies conducted in India. From these we have derived the major risk factors for CVD. This includes smoking, hypertension, abnormal lipids, high waist hip ratio, sedentary life style, psychosocial stress, lack of activity and low consumption of fruits and vegetables[2].

Obesity is a greatly evolving pandemic health problem. It is also said to be one of the most neglected health problems in the world[3].It is defined as a state of excessive accumulation of adipose tissue mass and is best viewed as a syndrome or a group of diseases rather than as a single disease entity. High body mass has been considered as the 6th leading cause of burden related with disability adjusted life years (DALYs) and also accounting for 3 million deaths[4]. According to WHO, obesity is defined as increase in body fatness >25% for men and >35% for women[5]. In other words, it can be said as weight exceeding 10% of standard weight.

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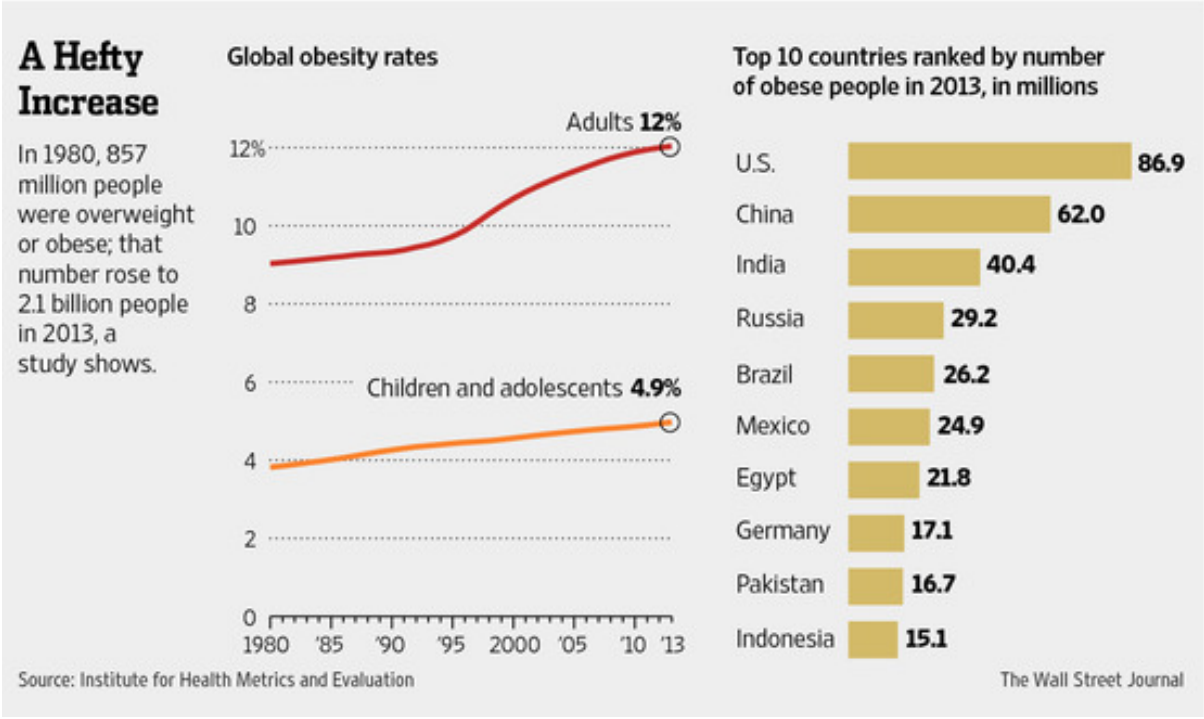
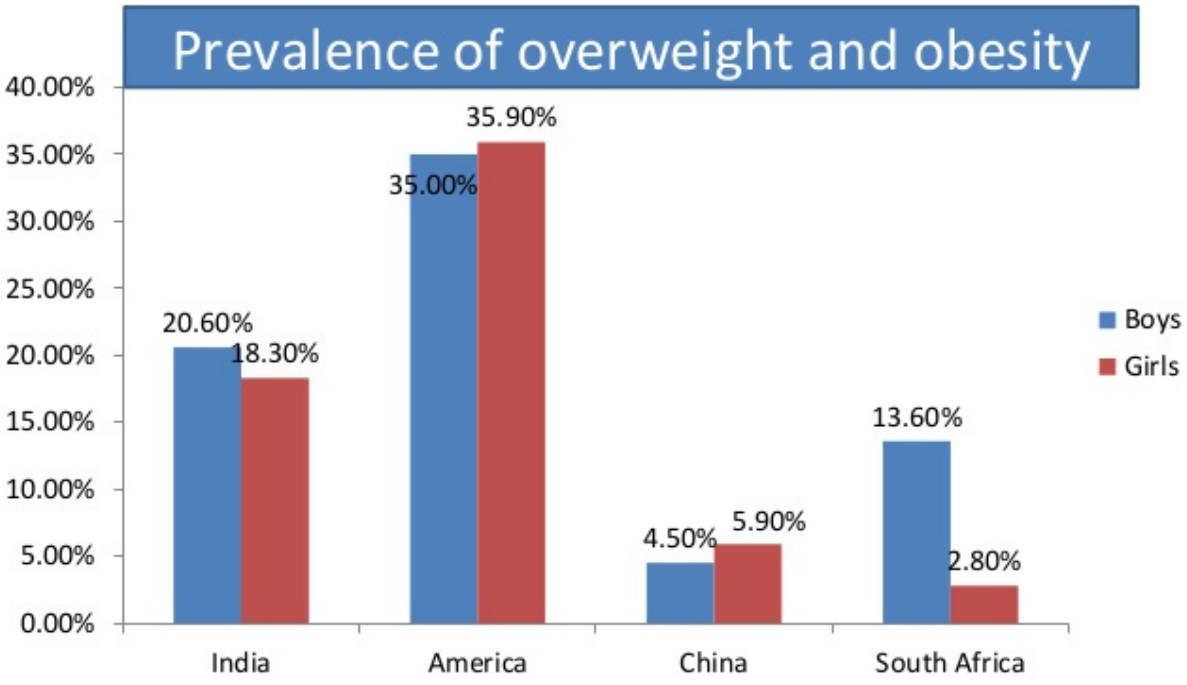
India ranks three in the top ten countries with obese people with a count of 40.4 million. This shows the ongoing obesity burden to India. Obesity leads to many kinds of complications like heart disease, stroke, degenerative joint diseases, hypertension, diabetes mellitus and some cancers which can impair a person's quality of life and produces a major burden for the society. Among these, cardiovascular diseases produce the greatest morbidity and mortality [7]. Obesity related mortality is mainly due to type 2 diabetes. All the cardiovascular disease risks are put under a single category called metabolic syndrome.



Global and Indian Scenario



Obesity now has a major predilection towards children and adolescents. This shows that the current trends will accelerate with time because they are the future generation. According to WHO report in 2005, approximately 1.6 billion people were overweight and at least 400 million adult populations were obese globally. It was also projected that by 2015, approximately 2.3 billion adults will be overweight and that at least 700 million will be obese[8]. The high prevalence of obesity is of concern in many perspectives.

Over the past 2 decades BMI was considered as a superior tool in correlating the effect of weight with morbidity and mortality. For adults, BMI cut-off values are age independent and same for both sexes. Obesity is derived differently for adults and children. Lower BMI thresholds are adopted for overweight and obesity for the Asia- Pacific region since this population has a greater risk for diabetes mellitus and abnormal lipid profiles even at lower body weight.

BMI & OBESITY CLASSIFICATION – WHO Criteria

	Obesity Class	BMI
Underweight		< 18.5
Normal		18.5 – 24.9
Overweight		25 - 29.9
Obesity	I	30 – 34.9
	II	35 – 39.9
Extreme Obesity	III	> 40

Universal cut off points are not appropriate for worldwide use because population specific and ethnic specific risks are prevailing. WHO Expert consultation concluded that Asian populations have a higher risk even at lower BMI. The cut-off point for observed risk varies from 22 to 25kg/m^2 and for higher risk starts from 26 to 31 kg/m^2. BMI greater than 23kg/m^2 are said to be overweight and greater than 25kg/m^2 are said to be obese for Asian Indians[9,10]. Now many studies have shown that the risk of cardiovascular illness not only depend on the excess weight per se but rather on the location of deposition of the excess fat. BMI fails to show the location of fat distribution. It just signals general fat deposition.

In light of this, it is now found that abdominal obesity (central obesity or android obesity or upper body obesity) is the type of obesity which is most likely to be associated with an altered risk factor profile contributing to an increased CVD and type 2 diabetes risk, while gynoid obesity (or lower body obesity with fat located around the hips and buttocks) is seldom associated with such metabolic complications. This kind of central fat distribution is evident with the help of waist circumference.

From the era of modern medicine, it is now possible to quantify the amount of adipose tissue either directly or indirectly. Intra abdominal fat can be more accurately quantified by dual energy X-ray absorptiometry (DEXA) or computed tomography (CT) or Magnetic Resonance Imaging

(MRI) or Ultra Sonography (USG). With the development of computed tomography (CT scanners), it has even been possible to clearly distinguish two different depots of abdominal fat:

1) Intra-abdominal (visceral) obesity (excess fat in the abdominal cavity).

2) Abdominal subcutaneous fat (the fat located just under the skin).

Even though these imaging techniques are most effective, they are much expensive and complex. They cannot be adopted for routine clinical settings or for large population based study due to its methodological difficulties and its high cost. For practical purposes, we can rely on waist circumference (WC), WHR to predict the intra abdominal fat accumulation. Our body's overflowing excess energy is stored as fat in subcutaneous adipose tissue (SAT). Adiposopathy is defined as adipose tissue dysfunction caused by positive energy balance and sedentary life style in environmentally and genetically susceptible individuals. Energy overflow can cause accumulation of fat in various planes of our body like perivascular fat, myocardial fat and pericardial fat which may directly produce atherosclerotic cardiovascular disease.

Thus obesity consequences are linked to the amount of intra abdominal fat rather than fat at other areas like buttocks and hip[11]. Now it is our duty to detect this central obesity much earlier even by using simpler techniques like measuring WC and it can be considered in

clinical practice. Thereby we can reduce some obesity related health burden in the society.

In persons between the age of 20 and 44, obesity is associated with four fold increase in relative risk of diabetes[12]. The leading cause of death in people with diabetes is coronary heart disease. Obesity is an independent risk factor for cardiovascular disease like congestive failure and coronary heart disease [13]. This visceral obesity is associated with increased incidence of hypertension and atherogenic lipid profile both can increase the chance of cardiovascular disease [14,15]. Randomized control trials and large observational studies have shown that increased total cholesterol, serum triglycerides, low density lipoproteins, and reduced levels of high density lipoproteins are associated with increased risk of CHD[16]. Early detection and intervention of abnormal lipid levels are essential to reduce CHD risk in individuals with central obesity as they are atherogenic.

AIM

&

OBJECTIVES

AIM AND OBJECTIVES

Aim

To determine central obesity is the major predictor of cardiovascular disease risk in women

Objectives

- To study the prevalence of central obesity in women
- To correlate Waist Circumference (WC) and Fasting Blood sugar
- To correlate WC and lipid profile
- To correlate WC and blood pressure
- To correlate BMI with FBS, lipid profile and blood pressure
- To detect which anthropometric measurement had more correlation with these blood parameters and blood pressure

REVIEW
OF LITERATURE

FAT AS AN ORGAN

Adipose tissue is no longer a “neglected tissue” as the pathologist H.Gideon Wells presented in his well remembered article of 1940[17]. An old controversy was that the adipose tissue, simply a modification of highly vascularised loose connective tissue which may collect fat in its cells[18]. An adult of acceptable weight is found to have 30-50 billion fat cells.

EMBRYOLOGY

Fat has a distinct origin, even though it was considered to be modification of connective tissue.A lentiform area of characteristic structure clearly separated from the surrounding connective tissue by a thin capsule. These bodies consist of network of capillaries and of mesenchymal cells. The cells are the prospective fat cells; nowhere except in these cells will fat appear and the entire formation will become a lobule of adipose tissue. The origin of these precursors of fat lobules can be traced back to small blood vessels; their endothelium produces the capillaries, while the mesenchymal adventitia spreads into the reticulum of the prospective fat cells. The developmental relationship between the anlagen of the fat cells and the blood vessels from which they derive had been demonstrated by Dabelow with India- ink injection of blood vessels.

From these findings, it was concluded that the adipose tissue originates lobule by lobule, from the reticuloendothelial organs, which

are the primitive organs of the fat lobules. These are produced by reaction of the local vascular mesenchyme. When fat depots develop in post embryonic life or under pathologic conditions, the process may be shortened in that cells begin to store fat during the spreading of the mesenchyme and the formation of the capillaries, while in the embryo the primitive organs are maintained for a short time before fat accumulates. The fundamental process is the same, a reaction of the vascular mesenchyme without which fat depots cannot be built.

HISTOLOGY

Adipose tissue is collection of connective tissue in which adipocytes or fat cells are predominating. It is located all over the body constituting 15-20% of the body weight in men while in women a little higher. Females have approximately 50% more fat cells than men. They serve as storage depots for neutral fats, key regulators of the body's energy metabolism.

There are two important properties of TGL which explain their selection as the preferred nutrient storage in need of energy demands and availability.

This includes 1) Fats are insoluble in water and they can be concentrated with no adverse osmotic effects on cells.

2) The caloric density of TGL is two fold higher than proteins and carbohydrates.

Adipocytes are largely active cells. They respond to both neural and hormonal stimuli. It is now recognized as an important endocrine tissue. It has peculiar physical properties like poor conductor of heat and helps in regulating thermal insulation. It also cushions the organs and helps in keeping the organs in its place. 85% of total adipose tissue mass is found to be under the skin. It is called subcutaneous fat. This layer of adipose tissue helps in shaping our body and also acts as shock absorbers in palms and soles. And a very smaller amount is seen within the abdomen. This is called intra-abdominal fat. It is present in both lean and obese persons. It is also called as visceral fat. This includes both retroperitoneal fat (drains into systemic circulation) and intraperitoneal fat (drains into portal circulation). Mesenteric and omental fat comes under intraperitoneal category[19].

Adipose tissue contains matrix of connective tissues among which white adipocytes appear in clusters or in singles. Adipose tissue has a shape of a signet ring, a metal band with a jewel or stone like nucleus present at the top.

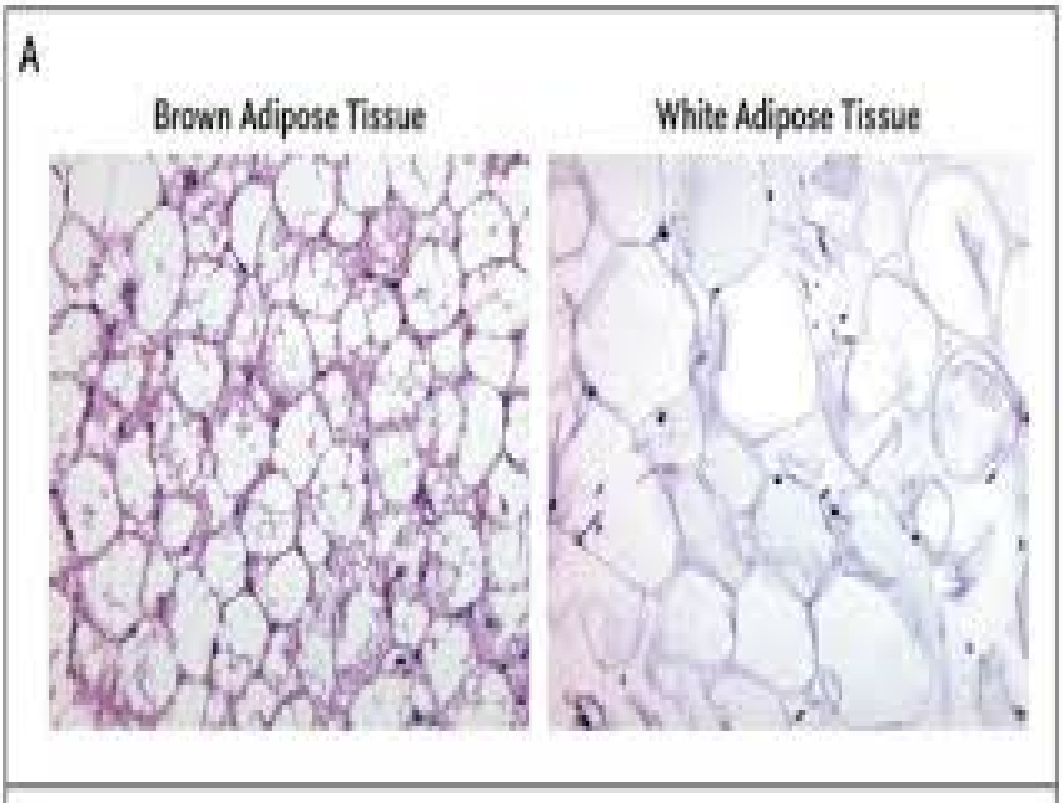
Two kinds of adipose tissue are white and brown adipose tissue.

White adipose tissue is the more common type. It is composed of cells that contain one very large droplet of whitish-yellow fat in their cytoplasm.

Brown adipose tissue contains abundant mitochondria and multiple lipid particles. It has a darker appearance and so it is called as brown adipose tissue. Both kinds of adipose tissue have a rich blood supply.

At birth, body of human infant contains 12% fat. It increases rapidly during the infantile period to reach a peak of 25% by 6 months of age. It then declines slowly over the next 10 years to 18%. At puberty, there is a significant increase in fat content in females, but it falls in males. By 18years of age females have 25 to 28% fat content in their whole body. In males it falls to 15% approximately. Between ages 20 and 50, fat content in females' increases by 50%.

ADIPOSE TISSUE



ADIPOSE CELLS IN OBESITY

The size of the adipocytes can increase up to 10 times when there is a need to store triglycerides. This kind of increase in fat cells is called as hypertrophy.

These increased fat sizes will bulge between strands of fibrous tissue producing a waffled and dimply appearance. These bulged areas are called cellulite. When the upper limit of fat storage is reached by hypertrophy then the fat cells now undergo hyperplasia. Hyperplasia means increase in number of cells. New adipocytes are developed from immature precursor cells. So an obese individual will have an increased number of adipocytes or enlarged adipocytes or both. They may have as many as 70-80billion fat cells. Once created, the number of fat cells cannot be reduced naturally. This is the reason why obese persons have a greater difficulty in losing weight once it has been achieved[20]. Liposuction is the only way by which these excess fat cells can be sucked out.

From birth to early adulthood period the size of fat cells will be doubled or even tripled. During the infantile period, most of the size increases. There is no significant change in fat size thereafter until puberty. There is no sex difference also. At puberty the fat size increases in females but it is almost constant in males. There also exists a difference in fat cells size depending on location. Visceral fat cells are

smaller than subcutaneous fat cells. Not all the subcutaneous fats are of same size. Fats in gluteal region are larger than abdominal adipocytes which again is larger than sub capsular cells.

OBESITY AND ITS TYPES

Since 1980, worldwide obesity has been doubled. As per WHO, obesity is defined as increase in body fatness >25% for men and >35% for women[21]. In other words, overweight and obesity are defined as abnormal or excessive accumulation of fat which may impair health.

In olden days, Obesity was classified according to the mechanism of production as,

1) Alimentary or exogenous obesity- due to excessive food intake

2) Constitutional or endogenous obesity- attributed to the hereditary constitution of the subject.

3) Endocrine obesity- due to disturbances in the functions of hypophysis (Cushing's disease), adrenals (Cushing syndrome), thyroid (hypothyroidism), gonads (menopause, castration).

4) Obesity due to brain lesions- like those of hypothalamus. It is called hypothalamic obesity.

Usually obesity is denoted by Body Mass Index (BMI). BMI has limited ability to tell about body fat distribution. Recently, the trend has changed towards the measure WC that can give information about

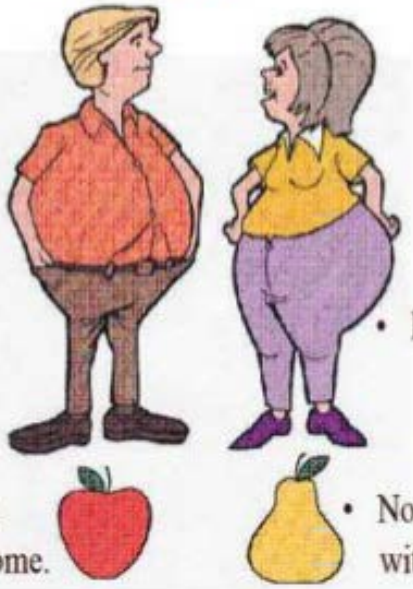
body fat distribution. That measurement is nothing but waist circumference. A person with central fat accumulation is more liable for cardiovascular complications. Obese persons also have psychological problems due to unattractive appearance and may also have sexual problems. Once it was the situation at which even though the women is said to have a higher body fat percentage than men they have a lower risk for cardiovascular disease because of their pear body shape[22]. But a recent report from Obesity update 2017 delivers a fact that, obesity is mainly affecting women due to social inequalities.

So based on area of fat storage, obesity is classified into 2 types: android (apple obesity) and gynoid (pear obesity). Recently a third type has been noted called, ovoid type. Dr.Jean Vague, a French Physician is credited with developing the terms “android” and “gynoid” obesity 50years ago[23].

ANDROID OBESITY

Here fat is mainly concentrated around the abdomen, chest and upper arms. This kind of distribution is seen mainly among men and results in an apple shape or central obesity. This kind of fat distribution has more risk for cardio metabolic events.

TYPES OF OBESITY – Are you an Apple or a Pear ??



Apple/Android

- Excess Fat on the Abdomen
- Common in Men
- Significant correlation with Metabolic Syndrome.

Pear/Gynoid

- Excess Fat on the thigh and buttocks
- Common in Women
- Non significant correlation with Metabolic Syndrome.

GYNOID OBESITY

This kind of Pear shaped physique is more common among women. Fat is more localized around hips, thighs. Overweight pear shaped obesity leads to mechanical stress in lower half of the body. This kind of obesity is less harmful because it is said that the adipose tissue in these areas are less metabolically active.

OVOID OBESITY

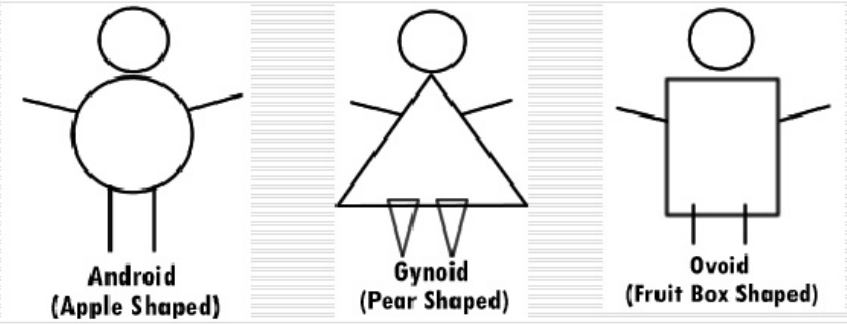
No differentiation between men and women kind of body fat distribution. This type of fat storage promotes an 'egg shape' fat distribution

For adults, the general WHO criteria for defining overweight and obesity as follows:

- Overweight is a BMI value which is greater than or equal to 25
- Obesity is a BMI value greater than or equal to 30

Globally, women have a higher prevalence of obesity than men[24]. As the BMI value is same for all ages and sexes of adults, it gives more information about the population level measure of obese and also overweight. But, it should be taken as a rough measure because of the fact that it may correspond to the same degree of fatness in different people.

Basic Somatotypes



It is logical to think that age should be considered while categorizing overweight and obesity. It is now said that those persons with increased lower body fat mass are protected from metabolic complications[25].

Many studies suggest that obesity can also exist even if the BMI is within normal limits. There is one kind of entity called “Normal Weight Obesity”. It is defined as a condition of having normal BMI but the percentage of body fat is high[26]. They are also called as TOFI (Thin on the outside fat on the Inside). TOFI are those people with BMI within normal limits with high intra-abdominal fat and thus more susceptible to DM. There is another entity called Fat fit phenotype. These people have greater BMI but metabolically normal[27].

At same BMI values, Asians of Indian origin tend to have 7-8% of higher percentage body fat than Europoids[28].

WAIST CIRCUMFERENCE:

WC is a kind of measurement of perimeter of the body which gives an estimate of body’s circumference at the abdominal level. WC can be measured at different anatomical landmarks like at 1) The level of umbilicus 2) just below the level of lowest palpable rib 3) Just above the iliac crest 4) midpoint between the lowest rib and iliac crest. The last

given site is usually taken as most acceptable because it is the site that has mainly evaluated the relationship between mortality, morbidity and obesity. But the site which is easily reproducible and identifiable is just above the iliac crest.

When we consider body as a cylinder, WC measures the circumference of the cylinder, length is from the height of the body, weight is a measure of mass. BMI gives more information about body mass and volume whereas WC gives details about body shape. WC also gives IAAT and SAAT volumes [29] but cannot say its individual contributions for which we need CT or MRI.

Waist circumference is highly correlated with abdominal fat and is used as a marker of central obesity. Waist circumference (WC) is a best predictor of health outcomes in adult men and women in all age groups and ethnicities like African, Asian, American, Hispanics and Caucasians. WC is an independent predictor of diabetes than BMI[30]. WC has a very strong correlation with diabetes risk. Cut off values for waist circumferences are different for different ethnicities because in some races like Indians a greater risk exists even at low level of BMI. These cut off values were derived from waist circumference that correlated with a BMI of 30kg/m^2 or even greater[31]. We people like Asians tend to have a higher body fat percentage for the same BMI and an increased prevalence of cardiovascular risk at lower BMI levels than Caucasians[32]. Added to

that, at any given WC, the relative risk for mortality is higher in Asians than in Europeans or African Americans[33].

World Health Organization (WHO) has indicated that threshold for WC which denotes increased risk in Asian population is 90cm for men and 80cm for women[34].

WC and WHR are independent of height and muscle mass of the individual. These two things are easier to measure and calculate. WC and WHR showed positive correlation with myocardial infarction than measures of BMI[35]. BMI associated risk is also influenced by racial and ethnicity differences. When matched on BMI, the risk for diabetes is much higher in Southeast Asian population than Whites[36]. A factor that modifies the risk of complications related to obesity is increase in weight during adulthood. Weight gain of about 5 kg during 18-20 years of life, increases the risk of developing hypertension, diabetes, CHD[37]. The risk of developing obesity associated complications can be modified by exercise like aerobic fitness. This will increase the maximum oxygen consumption and they have lower risk for developing complications. They have less chance of cardiovascular mortality[38].

MRI and CT are said to be the gold standard diagnostic tests to evaluate the quantity of subcutaneous adipose tissue (SAAT) and Intra abdominal adipose tissue (IAAT) [39]. In these methods cross sectional abdominal images are taken and then analyzed for amount of fat. The

most preferred level of slice to assess SAAT and IAAT is L4-L5 intervertebral level. But it does not provide the accurate value of total IAAT. For this assessment should be done several centimeters above the level of L4-L5 space. When IAAT volume is determined at the level of L1-L2 than at L4-L5 the association between metabolic syndrome and IAAT volume is much greater[40]. No universally accepted site has been evolved.

ANTHROPOMETRY

Obesity is a major rising problem in India. It was found that about 30-65% of the adults who were living in urban areas were found to be obese or overweight[41]. Anthropometry is the study of measurement of human body in terms of dimensions of bone, adipose tissue and muscle. The word anthropometry is derived from Greek word “anthropo” meaning human and metron meaning “measure”. Weight, stature, skin fold thickness, circumferences (head, waist, and limb), recumbent length, limb length and breadths (wrist and shoulder) are examples of anthropometric measures. Anthropometry is a key component of nutrition status assessment both in children and adults.

It was recommended by National Heart, Lung and Blood Institute that as an initial assessment WC should be measured and the value of WC can be used to follow up the efficacy of weight loss therapy in obese and also in overweight patients[30]

The ideal height weight table was first released by Metropolitan Life Insurance Company. The major purpose of this table was to determine life insurance rates based on studies of life expectancies. Those who overweighed were rejected when they applied for life insurance. This table was later adopted by medical team for purpose of public health. The term ideal body weight denotes a person's weight as compared to the weight in the ideal Height- Weight table.

ASSESSMENT OF OBESITY

1. Relative body weight:

   It is determined by the ratio of actual body weight with the desirable body weight in kilograms

2. Skin fold thickness:

   It is said that at least 85% of the body fat is located subcutaneously. So to measure body fat content skin fold thickness (SFT) is commonly used. It is inexpensive, easy to use in clinical and school setting and non invasive. Skin callipers are used for this purpose. For proper report, 12 measurements should be taken at 4 different sites. The commonly measured sites are biceps, triceps, and suprailiac, sub scapular. The three values at one site are averaged to give the result of that particular site. All these average values of the 4 sites are added together and compared with standard table to

determine the person's body fat. From the Indian data, studies suggest that SFT greater than 95th percentile to be considered as obese[42].

3. Body Mass Index(BMI) or Quetelet's index:

   It is the value obtained by dividing the actual body weight in kilograms by the height of the body in square meters. BMI is not used for body builders, pregnant women, elderly, long distance athletes and young children.

4. Waist Hip Ratio(WHR):

   It is the ratio obtained by dividing the circumference in centimetres of waist by the circumference in centimetres of hip.

5. Corpulence Index:

   It is determined by dividing actual body weight by desirable body weight.

   It should exceed 1.2 to say as obese

6. Broca's Index:

   Height of the body in centimetres- 100= Ideal weight.

SKIN FOLD THICKNESS

We have already discussed in detail about the waist circumference.

Percent reasonable body weight:

- Overweight: 10 to 20% above the reasonable body weight
- Obese: more than 20% above the reasonable body weight

The obese persons can be classified further as

- Mildly obese: 20-40% overweight
- Moderately obese: 41 to 100% overweight
- Severe (extremely): greater than 100% overweight

OTHER TECHNIQUES OF BODY COMPOSITION ASSESSMENT:

In the olden days, cadavers were dissected and studied about the body fat composition. But this technique is much difficult and problematic. Now, many new methods are available which includes hydrometry or dilution to determine total body water(TBW), densitometry (hydrostatic weight and air displacement plethysmography), dual energy X-Ray absorptiometry, computed tomography, magnetic resonance imaging, nuclear techniques like whole body counting of potassium 40 or neuron activation, ultrasound, total body electrical conductivity. All these investigations give more accurate value of body fat mass than the manual methods of measurement.

But all these procedures are costlier and cumbersome to be used. Accurate results are achieved with experienced hands only. The bioelectric Impedance Analysis evaluates body composition by measuring the distribution of fat in different parts of the body, differentiating them into tissue and fluid compartments. In athletic clubs and gyms electrical impedance is widely used. Subcutaneous fat often hinders heat loss by irradiation, and for this reason obese subjects perspire more than thin ones.

BIOLOGICAL MECHANISMS RESPONSIBLE FOR THE ASSOCIATION BETWEEN WC AND CARDIOMETABOLIC RISK

The relationship cannot be concluded with a single hypothesis. Many things are put forwarded to show their association.

- One of the earliest hypothesis which shows IAAT as a metabolic risk factor is that due to environmental stressors, central nervous system and adrenal axis gets activated producing preferential deposition of fat in the trunk areas and cardio metabolic disorders associated with that deposition[43].
- Another hypothesis is that subcutaneous tissue has limited ability to store excess energy. So whatever excess energy present will overflow to IAAT and ectopic energy storing sites like skeletal

muscle and liver. Excessive accumulation of fat in these ectopic sites produces metabolic dysfunction in such organs. Increased intrahepatic fat produce hepatic insulin resistance and also dyslipidemia[44]. Increased intra myocellular fat produce insulin resistance in skeletal muscle. From this statement we can say that IAAT is an index for overflow of fatty acids from subcutaneous adipose tissue.

- Metabolic products of omental and mesenteric fat tissue are released into portal vein which is directed towards the liver. These products produce hepatic insulin resistance and also provide substrate for synthesis of lipoproteins. The omental and mesenteric fat also produces certain hormones contributing to cardio metabolic risk.
- Fourth hypothesis is that, in some people there are presence of certain genes which causes preferential fat deposition in the abdominal areas can alone cause cardio metabolic risk.

PATHOGENESIS OF OBESITY

ENERGY BALANCE:

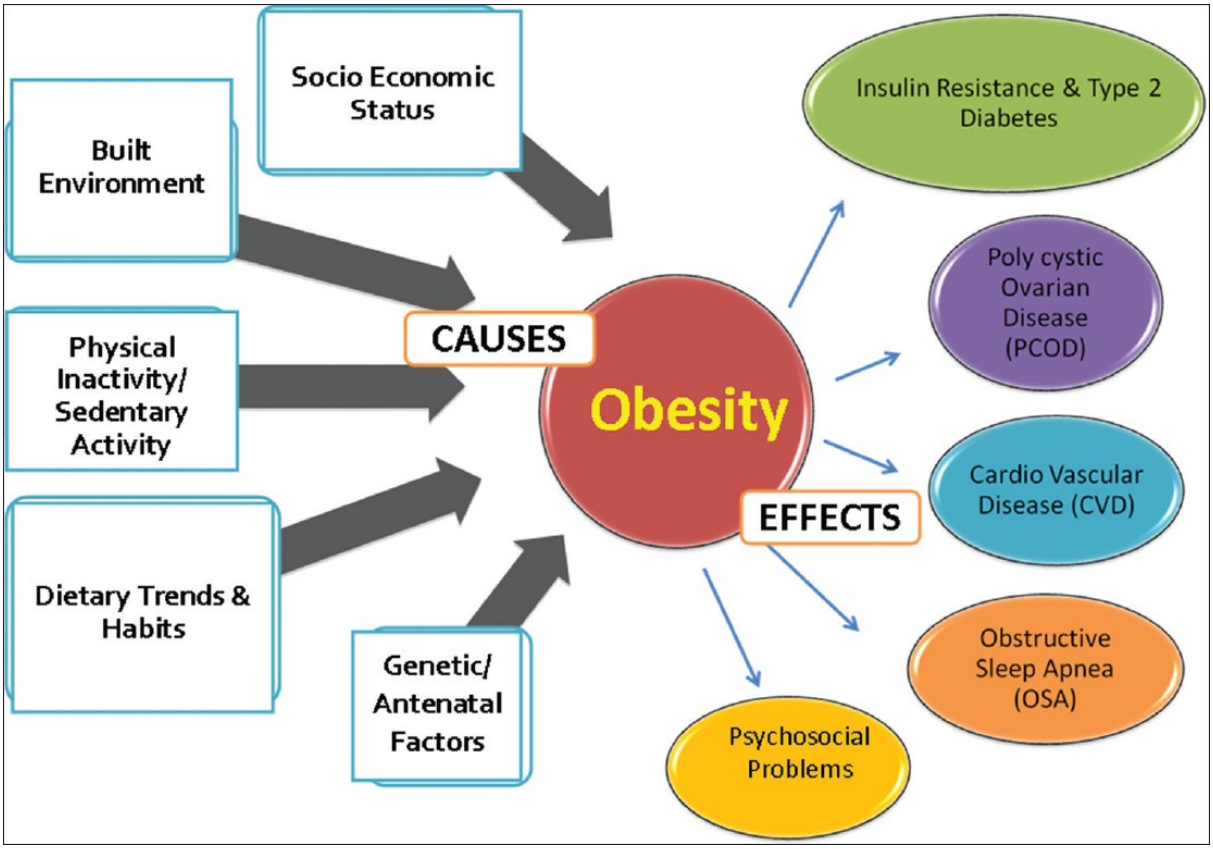
The major fundamental cause of obesity and overweight is an imbalance between calories consumed and calories expended. Worldwide, there has been an increased intake of dense energy foods that are high in fat content. Gastrointestinal tract has the capacity to absorb

large quantity of nutrients. In 1 year, only 5% increase in caloric intake than energy expenditure will lead on to 5kg increase in weight in adipose tissue.

ROLE OF HORMONES:

Body weight regulation is also coordinated by hormones and neuronal circuit. When there is food deprivation, appetite increases, energy expenditure gets reduced. Similarly, when there is over feeding, appetite decreases, energy expenditure has to be increased. But the latter does not happen, instead over feeding leads to overweight and obesity when food is abundant and physical activity is limited.

A major hormone regulating these adaptations is LEPTIN, which is an adipocyte derived hormone. Other major hormonal signals are insulin, gut peptides and cortisol. Neuropeptide YY, Agouti related peptide, Melanocyte concentrating hormone, cortisol, Ghrelin all these hormones stimulate appetite. MSH, Leptin, will decrease appetite. Another hormone which needs special mention is Peptide tyrosine (PYY3-36). This PYY3-36 is produced in the gut cells and their production is proportional to the kcal intake. This hormone is particularly produced after a meal and signals the brain, that the body is no longer hungry. So there should be a balance between the hormones which increase and decrease food intake.


Socio Economic Status
Built Environment
Physical Inactivity/ Sedentary Activity
Dietary Trends & Habits
Genetic/ Antenatal Factors
CAUSES
Obesity
EFFECTS
Insulin Resistance & Type 2 Diabetes
Poly cystic Ovarian Disease (PCOD)
Cardio Vascular Disease (CVD)
Obstructive Sleep Apnea (OSA)
Psychosocial Problems

GENES AND ENVIRONMENT:

Our body size depends on the complex interaction between environmental factors and genetic background. Only 40% variance in body mass is explained by genetic background in humans [45]. The major reason for a recent trend in obesity is due to alterations in environmental factors that increase energy intake and reduced energy expenditure by reduced physical activity. Now people are more interested to take restaurant foods and greater preference of snack foods, serving sizes are larger and also because of sedentary life style physical activity has considerably reduced.

Persons of genetic background are more prone for weight gain and develop obesity related diseases when they are exposed to a modern lifestyle during their life time.

Weight Maintained

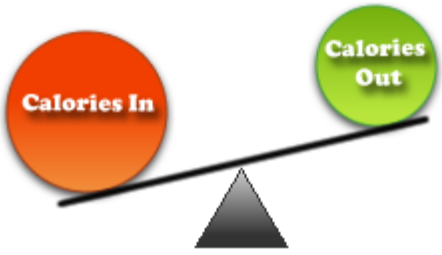
Isocaloric Balance

Energy In = Energy Out

Weight Loss

Negative Caloric Balance

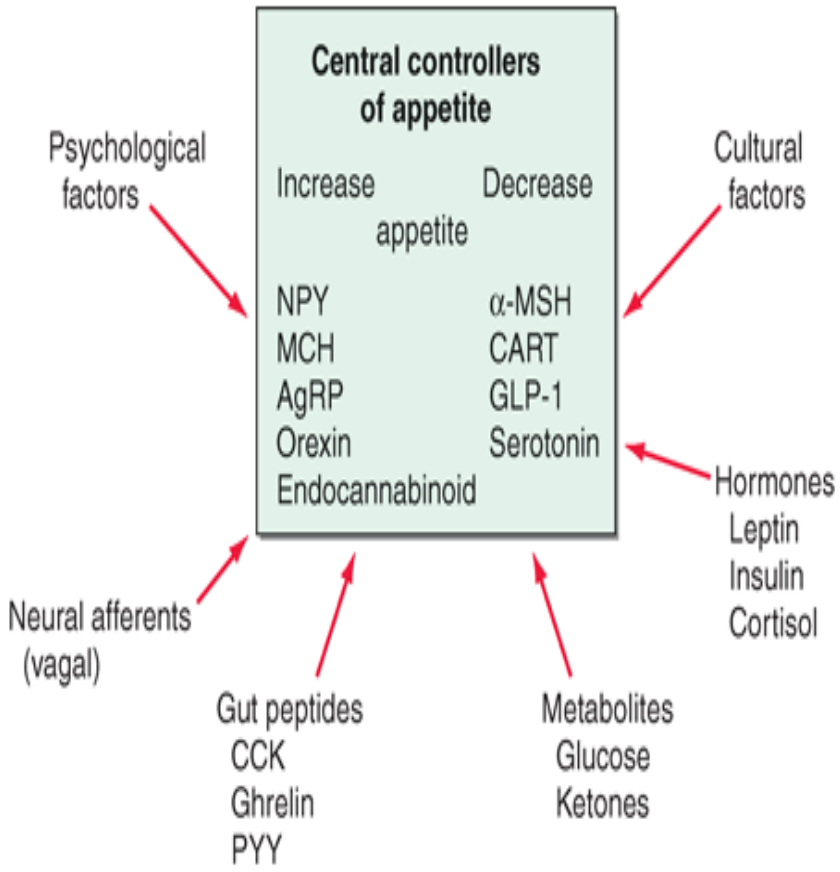
Energy In < Energy Out



Weight Gain

Positive Caloric Balance

Energy In > Energy Out


Central controllers of appetite
Increase appetite
Decrease appetite
NPY
MCH
AgRP
Orexin
Endocannabinoid
α-MSH
CART
GLP-1
Serotonin
Psychological factors
Cultural factors
Hormones
Leptin
Insulin
Cortisol
Neural afferents (vagal)
Gut peptides
CCK
Ghrelin
PYY
Metabolites
Glucose
Ketones

INFLUENCES OF CHILDHOOD AND PARENTAL OBESITY

The risk of getting obesity in adulthood also depends on being obese as a child or having at least one obese parent. This risk increases with increasing age and with degree of childhood obesity.

MONOGENIC CAUSES OF OBESITY

After the discovery of leptin, an adipose tissue protein, studies are going on to understand the molecular basis of body-fat regulation.

Leptin gene mutation:

Leptin is a hormone secreted by adipose tissue. It has 14 amino acids. The pathophysiologic relevance of leptin was studied in two extremely obese Pakistani cousins. They belonged to a consanguineous family. They were found to have a frame shift mutation of leptin coding region and premature leptin synthesis termination. Leptin treatment successfully reversed the condition. Serum leptin levels increase exponentially with fat mass, which shows that in obesity there is insensitivity to leptin resulting in body fat deregulation[46].

Leptin receptor mutation:

Mutation in leptin receptor gene resulted in hypogonadotropic hypogonadism, failure of pubertal development, secondary hypothyroidism, and delay in growth. These findings confirm the importance of leptin in endocrine regulation of energy balance and hypothalamic functions in humans.

Certain other mutations leading to obesity are pro-opiomelanocortin gene mutation, melanocortin 4 receptor mutations, prohormone convertase 1 gene mutation and mutation of Neurotrophin receptor TrkB.

POLYGENIC CAUSES OF OBESITY

Obesity may result from gene –environment interactions or due to gene-gene interactions. The major breakthrough given by genome-wide association studies was the discovery of fat mass and obesity associated gene (FTO). Many studies have shown that a strong association between single nucleotide polymorphism in FTO gene and fat mass (BMI) in both adult and childhood obesity. This single nucleotide polymorphism in FTO gene is strongly associated with type 2 DM[47].

ENERGY METABOLISM

Total daily energy expenditure (TEE) includes resting energy expenditure (REE) (70%), thermic effect of food (10%), energy expended during physical activity (20%). REE denotes the energy expended for normal organ and cellular function during post absorptive resting state. Thermic effect of food (TEF) denotes the energy expended in digestion, absorption and activation of sympathetic nervous system after ingestion of a meal. Energy expended in physical activity includes energy expended during exercise, spontaneous muscle contraction and posture maintenance. Certain studies have shown that obese persons usually have higher REE than lean persons of same height because obese subjects tend

to have a greater lean and adipose tissue cell mass[48]. In non weight bearing activities like cycling, obese persons expend same amount of energy as the lean persons. But in weight bearing activities obese persons expend more energy than lean ones, as more work is needed to carry their increased weight of the body[49].

Other syndromes associated with obesity:

Cushing, prader willi syndrome, Laurence –Moon- Biedl syndrome, Cohen's syndrome, Carpenter's syndrome.

OBESITY AND EVOLUTION

Are there any evolutionary roots to obesity?

In the modern obesogenic environment, those who have inherited the ancestral energy conserving genes have a genetic risk of developing overweight/obesity and associated chronic diseases[50]. However, this phenomenon of thrifty genes as proposed by Neel in 1962 has been contradicted by some authors[51]. Controversies and contradictions apart, obesity seems to have some evolutionary basis that has become a point of major concern for modern humans.

COMMON HEALTH CONSEQUENCES OF OVERWEIGHT AND OBESITY

Increased BMI is one of the major risk factor for noncommunicable diseases like:

- Cardiovascular diseases mainly stroke and heart disease. This was the leading cause of death in 2012 as per WHO report
- Diabetes
- Musculoskeletal disorders like osteoarthritis
- Cancers involving various organs.

The risk for these diseases increases with increasing BMI. Childhood obesity has a higher chance of obesity in adult, disability in adulthood and premature death. In addition to these risks, obese children will have breathing difficulties, fracture risks, hypertension, and psychological effects.

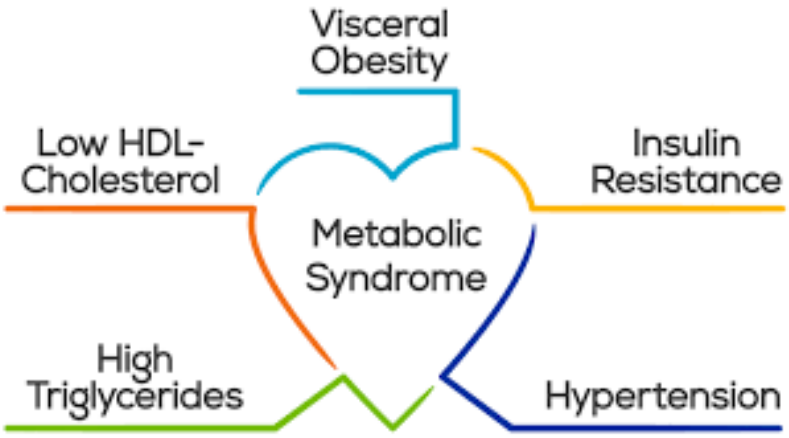
THEORY OF OBESITY

There are many theories which describe obesity but none is true for everyone. For each one the reason may be different. Researchers have shown that obese mice have a deficiency of hormone leptin. The gene responsible for hormone leptin is ob gene. It helps to prevent obesity. Leptin acts as adipostat by signaling the brain regarding body fat stores. When exogenous leptin is administered to leptin deficient rodents, it causes decreased food intake, weight loss and increased metabolic activity. In some obese persons the level of leptin will be very high which shows that they are leptin resistant. This discovery dampens the use of leptin in treatment of obesity. Leptin is considered as afferent satiety signal.

The Driving force for metabolic syndrome: OBESITY

Obesity is a condition where excessive fat accumulation occurs to such an extent that health and well being are affected adversely.

The prevalence of obesity increases the prevalence of metabolic syndrome[52]. High carbohydrate diets with rich in glycemic index are said to worsen metabolic syndrome. Adipose tissue plays a key role in metabolic syndrome[53]**.** Non esterified fatty acid (NEFA) is the key fuel source. In fasting state, adipose tissue triglyceride undergoes lipolysis and releases NEFA into circulation. The enzyme involved in lipolysis is hormone sensitive lipase. This enzyme activity is enhanced by nor epinephrine and suppressed by insulin. During fasting, when the insulin level is low, lipolysis is not inhibited and more release of NEFA into circulation. Lipids start to accumulate in muscle and liver when NEFA supply exceeds the energy needs. All these changes added with metabolic alterations leads to metabolic syndrome.


Visceral Obesity
Low HDL-Cholesterol
Insulin Resistance
Metabolic Syndrome
High Triglycerides
Hypertension

METABOLIC SUSCEPTIBILITY: Dysfunctional adipose tissue:

Four potential disorders that can accentuate metabolic syndrome include genetic forms of insulin resistance, subcutaneous adipose tissue, inflammation of adipose tissue and dysfunctional adipose tissue.

A severe deficiency of adipose tissue is called lipodystrophy[54]. In lipodystrophy fat starts to accumulate ectopically in liver and muscle. It results in severe metabolic syndrome.

Insulin is a major regulator of metabolism of adipose tissue. When there is genetic defect in insulin signaling, lipolysis suppression will be impaired. Adiponectin release will be reduced[55]. Adiponectin favors insulin sensitivity. Insulin resistant dysfunctional adipose tissue people will have high CRP, high leptin levels and increased NEFA, low adiponectin –even they are not obese. These persons are prone to premature type 2 DM and metabolic syndrome. In obese persons, macrophages will invade adipose tissue[56]. Release of inflammatory cytokines will occur when there is activation of these macrophages. The cytokines causes insulin resistance.

MANAGEMENT OF OBESITY

Energy

For a sedentary person about 20Kcals per kg of body weight is prescribed and about 25Kcals per kg body weight for moderately active

person. Food energy intake should not be more than what is necessary for expenditure. It should always be lesser than energy consumed.

The most common methods for reducing obesity are as follows

1. Dietary control
2. Exercise
3. Drug therapy

Dietary control

The quantity of food which one is taking should be halved to start with. Initially it should be of 100Kcals and it should contain a large amount of fibers. Small quantities of food should be taken frequently to control appetite and one should eat food slowly than to gulp it down in hurry. Diet should contain 1gm of protein per kg of ideal body weight. Ghee, butter, eggs, fried foods and fatty preparations, sweets, potatoes and alcohol should be avoided. Vegetable oils except coconut and palm oil may be consumed to provide the required essential fatty acids. Lightly prepared soup like preparations, green vegetables as spinach, bathua, cabbage, coriander, spearmint, fenugreek leaves, bottle gourd, ridge gourd, or ribbed gourd, salad and fresh fruits should be included in diet. Cucumber and or tomatoes should be taken in between the principle meals to prevent hunger. Skimmed milk should be taken.

Salt intake should be restricted. No extra salt should be added.

Fluid should be taken in abundance as they give feeling of filling sensation. A glass of water consumed before a meal lessens the food intake.

On dieting weight of the body is lost rapidly, say ½ to 2 pounds per week for about 6 months. Initially this is due to loss of excess water content of the body as evidenced by increased frequency of micturition and polyuria. Therefore, the weight is somewhat stationary for a few months, when one adopts oneself to new weight and then one starts to lose weight again. In this way, when desired weight is reached, one should maintain it.

Exercise:

Generally, obese persons lead sedentary life style. They have to lose their body weight. For this purpose, a low caloric diet with moderate exercise as walking for increasing calorie expenditure should be advised.

Brisk walking for 30-45 minutes with pleasure daily in the morning and evening is to be insisted. Walking at a speed of about 5kilometers per hour will involve expenditure of 300Kcals in one hour. Moreover, obese persons can also take part in light outdoor games such as badminton, table tennis, swimming and cycling etc. This will provide exercise, entertainment, close company and at the same time will prevent social isolation. For housewives household activities like mopping, sweeping

the floor, cleaning the utensils and gardening etc are the forms of exercise.

Drugs

Laxative- Patient should take husk of isubghol 2-3 teaspoonful with milk at bed time or some other laxative containing fibers in abundance should be taken.

Anti-obesity drugs-

1. Amphetamine sulphate- it is anorexic i.e causes loss of appetite in obese patients but is not very effective as its large doses are toxic and its prolonged use may cause dependence.
2. Fenfluramine hydrochloride- It is mostly used in medicine in obesity which acts by causing loss of appetite like amphetamine but has many side effects like dryness of mouth, palpitation, insomnia, depression and hypertension and drug dependence. So it should not be given in case of hypertension, heart disease, epilepsy and pregnancy.
3. Phentermine- it is also an anorexic used as a single capsule daily
4. Diethylproplon hydrochloride- it acts like amphetamines in the treatment of obesity.
5. Orlistat- It is a drug approved by the food and drug authority of USA for the treatment of obesity by reducing fat absorption from the gastrointestinal tract.

Surgical Treatment

1. Liposuction- Excess of fat from the body is removed but it is generally associated with recurrence and a few complications.
2. Gastric plication- Some surgical staples are placed across the upper portion of the stomach due to which the capacity of food intake is reduced.

PANCREAS

The word pancreas derived from Greek which means all flesh. Pancreas has both an exocrine and endocrine part which is a unique feature of this organ.

EMBRYOLOGY

The endocrine part of pancreas consists of islets and the exocrine part is formed by acinar cells. Embryologically, it originates from ventral and dorsal regions of foregut endoderm as ventral and dorsal pancreatic buds on days 32 and 26 respectively. These buds will fuse at 36 days to form pancreas[57]. The posterior part of head of pancreas develops from ventral bud while the remaining part of the organ develops from the dorsal bud. By 12^{th} week islets are identified in human embryo. They have own independent blood supply. Their function starts by 16^{th} week[57]. There are two types of islets, A cell rich and F cell rich islets. Basically, A cell rich develops from dorsal pancreatic bud and F cell rich islet

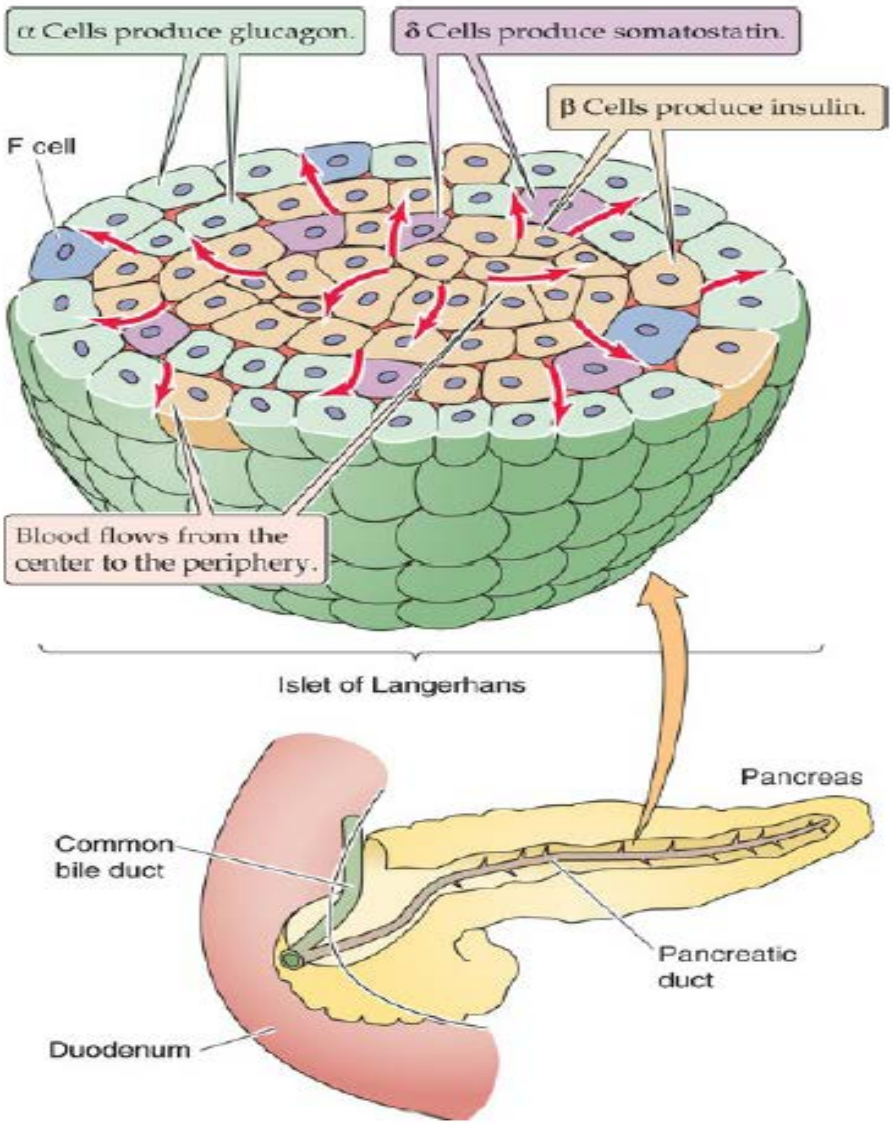
secrete more amount of pancreatic polypeptide develops from ventral pancreatic bud[58].

ENDOCRINE PANCREAS

The endocrine function of the pancreas is performed by variety of cells present in the islets of Langerhans. These islet cells were discovered by Paul Langerhans, German physician in 1869. These are tight aggregation of cells embedded in exocrine tissues of pancreas. Four cell types in islets: α cells, β cells, δ cells and PP (pancreatic peptide) cells also called γ cells. The β cells constitute major population and secrete insulin, the insulin antagonist amylin and some other peptides.

Insulin release is stimulated by hormones like glucagon, gastric inhibitory peptide, epinephrine, and increased blood glucose and amino acid levels. B cells are polyhedral in shape and secretory granules are packed in it. α cells secrete glucagon, δ cells secrete somatostatin and γ cells secrete pancreatic polypeptide. In most mammals, β cells lie at the centre which is surrounded by a thin layer of α, δ, and PP cells. It is about one to three cell thick[59]. In humans, the concentric segregation of cells is less defined with sometimes islets taking the shape of oval and cloverleaf pattern. In the islets of mature pancreas β cells constitute 70-80% of islet mass. There are about 3, 00,000 -1.5million islets present in the pancreas of an adult 70Kg man.

CELLS OF PANCREAS



INSULIN BIOSYNTHESIS

Insulin was first isolated from pancreatic tissue in 1921 by Banting and Best[60]. In mammals, expression of insulin gene and insulin biosynthesis is restricted to the β cells of pancreas[61] with possible exception of the fetal liver and yolk sac. The main function of β cell is the production, storage and regulated secretion of insulin. There is always a readily available pool of insulin to meet any sudden increase in glucose load. Its release is compensated by insulin biosynthesis. Insulin is a peptide hormone. It is synthesized as preprohormone in rough endoplasmic reticulum. It is then converted to prohormone. This conversion also occurs in rough endoplasmic reticulum by an enzyme called signal peptidase.

This proteolysis arises for the most part cotranslationally, so that preproinsulin composition in the β cell is very minimal.

REGULATION OF INSULIN BIOSYNTHESIS

The rate of biosynthesis of proinsulin is controlled by factors like nutrients, hormones and neurotransmitters. Of the various factors the most important is the glucose[62]. The threshold concentration of glucose required to stimulate biosynthesis of insulin is found to be between 2-4 mM and that required to induce insulin secretion is between 4-6mM[63]

When the blood glucose concentration reaches 10-12 mM, the proinsulin biosynthesis attains a maximum concentration. There is a time lag of 20 minutes between the stimulation of β cell with glucose load and significant increase in proinsulin biosynthesis. Its rate is increased to 10-20 folds by 60minutes. Some other hormones like growth hormone, glucagon like peptide-1and glucagon also stimulate insulin biosynthesis. The hormones like glucagon and glucagon like peptide stimulate insulin biosynthesis via cAMP dependent pathway. The rate of proinsulin biosynthesis is increased in obesity[64] but there is increase in β cell mass and there is islet cell hyperplasia in obesity. Extracellular Ca^{2+} is needed for insulin release due to glucose but proinsulin biosynthesis is independent of calcium[65]. Mg2+ appears to be needed for proinsulin biosynthesis but not for insulin release. Long chain fatty acids markedly potentiate insulin release. Rough endoplasmic reticulum is the major site of proinsulin biosynthesis. The earliest form of secretory granule in the β cells is formed in the regions of trans-Golgi. This region is characterized by presence of clathrin on their cytosolic surface. It is found that clathrin is involved in purging of unwanted proteins from the secretory granules during their process of maturation. The conversion of proinsulin to insulin and C-peptide occurs in the clathrin coated immature secretory granule.

NORMAL β CELL FUNCTION:

The storage and metabolism of cellular fuels is regulated by the pancreatic β cell through their insulin secretion. This is done by a feedback loop: glycemia causes β cell to secrete insulin; proinsulin biosynthesis occurs; then conversion of proinsulin to insulin takes place; and the secreted insulin in turn lowers plasma glucose by increasing glucose uptake into target cells like skeletal muscle. Insulin secretion occurs in pulsatile manner with a periodicity of 11-14minutes. This is necessary to fully regulate hepatic glucose production[66]. There also several large bursts of insulin release occur with meals, which will increase the efficiency of nutrient clearance. Oscillatory pattern of insulin secretion is called entrainment[67]. Failure of this entrainment has been proved as an early defect in insulin secretion which precedes abnormalities in traditional tests. C-peptide is secreted in equimolar ratio with insulin but it undergoes minimal hepatic degradation and thus C-peptide can be used for estimating the true rate of insulin secretion.

β cell dysfunction in type 2 DM

The proportion of patients with type 2 diabetes mellitus is increasing day by day. WHO predicts that incidence of type2DM will rise up to 300 million by the end of 2025[68]. T2DM mostly associated with obesity, aging, a high fat diet, inactivity or genetic basis. All these factors

will lead to insulin resistance. β cell function is always affected in T2DM. Its dysfunction occurs earlier and thus hyperglycemias are predated[69]. There is very little change in insulin resistance during the progression from impaired glucose tolerance to DM but there is a substantial change in β cell function. β cell failure coincides with progression from IGT to overt diabetes[70]. Even after the onset of diabetes, β cell dysfunction is reversible to a great extent by intense glycemic control[71].

SECRETION OF INSULIN IN TYPE 2 DM

It's a common finding of obesity pairing with insulin resistance. They are found to have hyperinsulinemia but the degree of hyperinsulinemia is inappropriately low for the plasma glucose concentration. Nevertheless, these patients have sufficient β cell reserve to maintain a normal glucose level by dietary restriction with or without an oral hypoglycemic drug. It is found that there are defects in β cell function of pancreas on the background of insulin resistance which both these things converge to form type 2DM. In a study with animal model with hyperinsulinemia, obesity, and insulin resistance, before the development of diabetes mellitus, inadequate expansion of β cell mass was a significant causative factor. Human autopsy findings also support this study. These patients have absent first phase insulin and C-peptide responses to intravenous glucose, second phase response are also

reduced, and glucose-insulin secretion dose-response curve shows a marked flattening[72]. However, this abnormal first phase response persists in patients even after strict glycemic control further supporting the presence of an intrinsic defect in β cell in patients with type 2 DM. Some studies consistently showed that elevated levels of proinsulin in association with increases in the molar ratio of proinsulin to insulin; which means that β cells of patients with type 2DM release excess of immature secretory granules into the circulation. The amount of proinsulin secreted in these patients appears to be related to the degree of glycemic control and it does not depend on the duration of diabetes. So hyperinsulinemia reported in cases with type 2 DM to some extent represents hyperproinsulinemia rather than true hyperinsulinemia. In a 24 hour period, patients with type 2 DM have a higher basal level secretion of insulin. Postprandially there is a reduction in the proportion of insulin secreted because the amplitude of secretory pulses of insulin is reduced rather than the reduction in the number of pulses. Improvements in diabetic control will regain β cell secretory activity[73].

INSULIN SECRETION IN OBESITY

Resistance to insulin in obesity is characterized by hyperinsulinemia. It may be due to a combination of increased production of insulin and reduced clearance of insulin. Both the 24-hour insulin secretion and basal secretory rates of insulin are 3-4 fold higher in obese cases and it strongly correlates with body mass index. At any instance, for each level of plasma glucose secretion of insulin rate are much higher in insulin resistant subjects, which shows an adaptive response of the β cell to peripheral insulin resistance. In the obese patients, basal secretion of insulin provides 50% of the total daily production of insulin and once in every 1.5-2 hours secretory pulses of insulin occur[74]. But however, in obese patients, the amplitude of these pulses is greater postprandially. It was found, that the increase in insulin secretion in obese patients are due to the presence of large functional β cell mass rather than the hyper-responsiveness to secretory stimuli.

INSULIN RESISTANCE IN OBESITY

In obesity, there will be resistance to the effect of insulin in uptake, metabolism and storage of glucose. Resistance to insulin is one of the major pathogenic problems in type 2 diabetes and is often associated with other major pathogenic states like hyperlipidemia, hypertension, atherosclerosis and polycystic ovarian disease. A newer concept is that

resistance to insulin and hypeinsulinemia may actually contribute to development of obesity than being as a cause of obesity. The link is at the fat cell level itself. It is proposed that hyperinsulinemia activates an enzyme called 11β-hydroxysteroid dehydrogenase in adipose tissue of omental site. This will generate active cortisol and promotes cushingoid type of fat distribution[75]. This insulin resistance in obesity and type 2 diabetes manifests mainly by decrease in insulin stimulated uptake of glucose and its metabolism in skeletal muscle and adipocytes and by decrease in insulin mediated suppression of hepatic glucose output. This is mainly due to down regulation of insulin responsive glucose transporter- GLUT4. In both these target organs (skeletal muscle and adipose tissue) the resistance to insulin results in reduction of insulin binding to its receptor, phosphorylation of its receptor, activation of tyrosine kinase and phosphorylation of insulin responsive substrate proteins.

The action of insulin to reduce the blood sugar level is by decreasing the hepatic production of glucose and increase in the uptake of glucose into fat and muscle. But majority of glucose disposal occurs in muscle than to fat. This is because muscle mass is much higher than the white adipose tissue mass, muscle provides a major outlet for glucose

disposal. Glucose disposal into brown adipose tissue is much higher than into muscle in adults.

It is also said that VAT is anatomically in contact with portal vein. So the liver is exposed to free fatty acid flux and impair glucose-insulin homeostasis. This decreases degradation of insulin in liver and decreases the utilization of glucose peripherally in obese people and so become more at risk for insulin resistance, T2DM and CVD[76].

IMPACT OF BODY FAT LOCATION ON INSULIN REISTANCE

Many studies have shown that the risk for diabetes and insulin resistance rises as body fat content increases from very lean to obese implying that dose of body fat has an effect on insulin sensitivity[77]. Although it is seen with measures of general adiposity such as BMI, all the sites of adiposity does not contribute to same levels of risk to diabetes. Central or intra abdominal fat depots are more commonly associated with diabetes and other cardiovascular diseases. This is because some biochemical feature of intra-abdominal adipocytes directly influences systemic sensitivity of insulin. A leading hypothesis is that adipocytes which are located in abdomen are lipolytically more active than elsewhere. The increased intraportal FFA levels and flux will hinder the clearance of insulin and promote resistance to insulin by mechanisms that are still unknown.. It was assumed that reduced clearance of insulin

can lead to hyperinsulinemia, this in turn can produce down regulation of insulin receptors and desensitizing post receptor signaling pathway. Another concept is that intra abdominal adipocytes secrete both quantitatively and qualitatively a different combinations of factors which lead on to derangement of insulin action systematically.

LIPOTOXICITY AS CAUSES OF INSULIN RESISTANCE

The term lipotoxicity has been coined in order to describe the negative impact of expanded adipose tissue depot in obesity. It also includes lipid accumulation in non adipose tissue. The excess fat accumulation in obesity leads to elevated plasma FFA and impaired hepatic metabolism. This elevated FFA impairs the ability of insulin to decrease the glucose output from liver, and stimulate glucose uptake into skeletal muscle and inhibit pancreatic insulin secretion.

DEFINITION OF DIABETES MELLITUS

Diabetes mellitus is a heterogeneous group of metabolic disorder characterized by elevated blood glucose and associated with disturbances in carbohydrate, fat and protein metabolism resulting from defect in secretion of insulin, action of insulin action or both[78].

Criteria for Diagnosing Diabetes Mellitus:

- Symptoms of DM plus blood glucose taken randomly> 200 mg/dl

- Blood glucose taken in fasting > 126 mg/dl
- 2 hour blood glucose > 200 mg/dl after an oral glucose tolerance test.

Any one of the above criteria can be used for diagnosing DM.

Diabetes is called as "STARVATION IN THE MIDST OF PLENTY". Because the extracellular glucose will be higher whereas intracellular glucose is low due to reduced entry of glucose into peripheral tissues. Basically diabetes can be classified as Type 1 DM, Type 2 DM, gestational DM (Type 3)

Type 1 DM is mainly due to autoimmune destruction of beta cells of islets leading to insulin deficiency. So it is also called insulin dependent DM. This mostly occurs before 20 years of age. In Type 2 DM, the major defect is insulin resistance and or insulin secretion. Insulin secretary defect is usually preceded by insulin resistance which led on to exhaustion of beta cells and produces insulin secretary defect. Diabetes develops when the insulin secretion becomes inadequate.

GENETIC CORRELATION IN TYPE 2 DM

Type 2 DM strongly correlates with genetic component. The concordance rate for the identical twins is 70 to 90%. Similarly if both the parents are diabetic the chance for the offspring to be a diabetic is 40%. Many genes have been identified in the causation of type 2 DM. Currently identified genes are inward rectifying potassium channel, Zinc

transporter, peroxisome proliferators-activated receptor γ(PPAR-γ) and the list continues.

LIPID METABOLISM IN DIABETES

Obese persons are more prone for diabetes. In a person with insulin insufficiency, marked changes in fat metabolism occur. There is decreased synthesis of fatty acids and triglycerides and decreased conversion of glucose to fats in adipose tissue. Mobilization and utilization of fats and fatty acids from fat depots is increased. With increased fat catabolism, the production of acetoacetic acid and its derivatives acetone, beta-hydroxybutyric acid is increased (ketogenesis). In diabetics, glucagon secretion is also increased and this contributes to many other metabolic effects.

BLOOD PRESSURE

The blood pressure which we usually measure using sphygmomanometer gives us useful information about cardiovascular status of a man. In the year 1828, mercury sphygmomanometer was discovered by Bernoulli.

It is the product of cardiac output and systemic vascular resistance. The cardiac output is increased in obese patients is due to increase in blood flow to the adipose tissue. Systemic vascular resistance also

increased due to factors like hyperinsulinemia, over activated sympathetic nervous system, disordered sleep pattern like sleep apnea. Increase in severity of obesity, worsen the blood pressure.

Systolic pressure: It is defined as the maximum pressure which is reached during the cardiac cycle. It indicates the force of contraction of heart. Thus it predicts the work done by the heart.

Diastolic pressure: It is defined as the minimum pressure attained during the cardiac cycle. It depends on the total peripheral resistance.

HYPERTENSION:

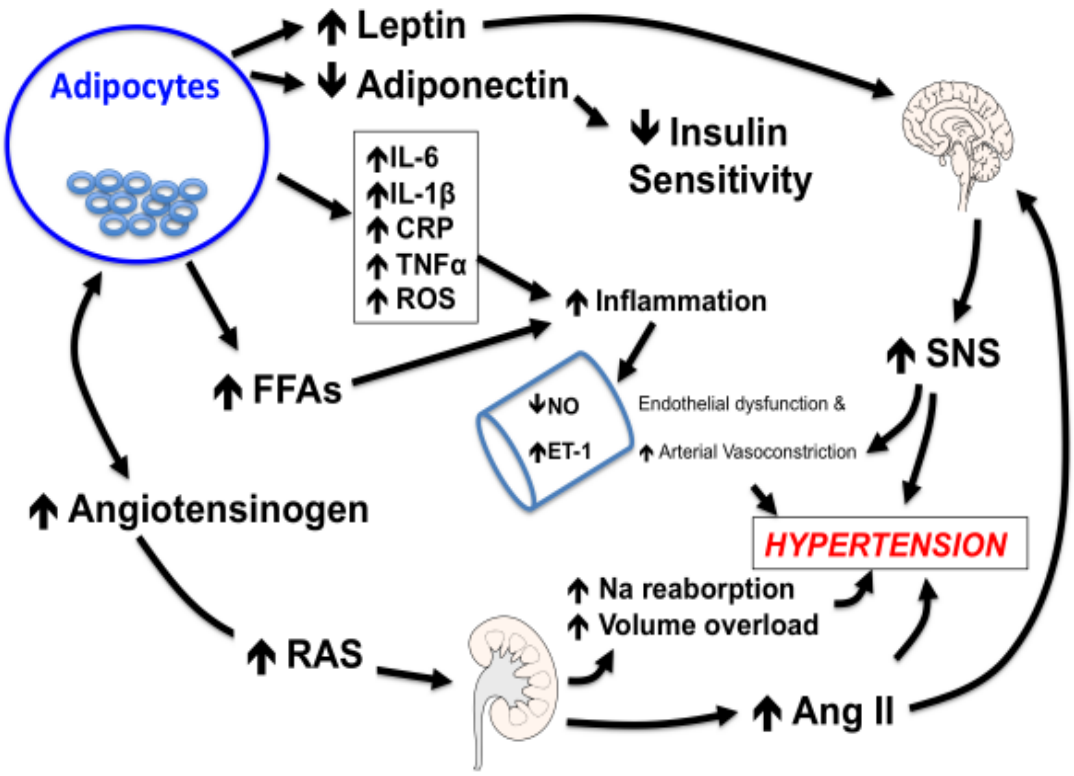
Nowadays, it has become a very common non communicable disease. It accounts for more than 85% of excess cardiovascular disease risk (CVD). Patients with hypertension are more prone to diabetes than those who are normotensives. Hypertension will further increase the risk for stroke, retinopathy and coronary heart disease. When both the diseases exist together the risk for CVD is doubled. Hypertension individuals with diabetes has a characteristic features like isolated systolic hypertension, loss of nocturnal dipping of blood pressure and pulse, volume expansion, increased salt sensitivity , albuminuria and increased tendency for orthostatic hypotension[79]. As per Framingham heart study, rise in systolic blood pressure by 20mm Hg and the risk for

cardiac failure increases by 56%. This was proposed by **Adler et al**[80]. In obese individuals, on the right side of the heart, there is increase in filling pressure, pulmonary vascular resistance also increases. Increased pulmonary vascular resistance may be due to hypoventilation, left ventricular dysfunction or any pulmonary disease. All these pathologies are more common in obese people. In obese people with obstructive sleep apnea, the condition is even made worse by nocturnal dysrhythmia, right heart failure, myocardial infarction, and stroke. Left ventricular diastolic dysfunction is more common than systolic dysfunction. When compared with normal people, subclinical changes in the structure and function of the left side of the heart particularly the left ventricle, such as differences in the regional or global strain, were identified in asymptomatic.

RELATIONSHIP BETWEEN HYPERTENSION AND DIABETES:

CVD is the major cause of death in patients with diabetes. It has been shown that hypertension leads to insulin resistance and further causes hyperinsulinemic state. In patients with essential hypertension, fasting and postprandial insulin levels were elevated independent of BMI and with a direct positive correlation between blood pressure and plasma insulin levels. It is concluded that hypertension is an insulin resistance state. But this association is not for secondary hypertension. It shows that there is a common genetic predisposition for diabetes and hypertension.

Mechanisms of Obesity-Induced Hypertension



One of the classical features of metabolic syndrome is high blood pressure. It has been shown that in one third of hypertensive patients metabolic syndrome exists**.**

MECHANISM FOR DEVELOPMENT OF HYPERTENSION

Visceral Obesity

Visceral obesity plays an important role in development of hypertension. Studies show that adipose tissue is a major endocrine organ that secretes adipocytokines. When a person develops obesity this secretion of adipocytokines get altered which lead to metabolic disorders. Accumulated visceral adipose tissue produce and secrete substances like IL-6, tumor necrosis factor (TNF)-α, non esterified fatty acids (NEFA), angiotensinogen, leptin, visfatin. All these factors lead to development of hypertension in metabolic syndrome. It is said that obesity is a common feature of patients with resistant hypertension and >40% patients with resistant hypertension are obese. Obesity also reduces the BP lowering effect of drugs.

INSULIN RESISTANCE

The main pathophysiologic feature of metabolic syndrome is insulin resistance. Insulin has an anti-natriuretic effect thereby causing renal sodium re-absorption. Even though there is resistance to the actions of insulin, the anti-natriuretic effect is preserved and produces hypertension in patients with metabolic syndrome. A study by **Strazzullo**

P, et al showed that in individuals with metabolic syndrome proximal fractional sodium re-absorption (FPRNa) was much greater than those without metabolic syndrome. Insulin also stimulates endothelin 1 production. Endothelin -1 act on the vessel wall and increases the blood pressure.

SYMPATHETIC OVERACTIVITY

In obese individuals serum catecholamines levels and muscle sympathetic nervous activity (MSNA) are found to be elevated. MSNA were significantly greater in central obesity individuals. Renin angiotensin system is activated thereby producing hypertension in obese patients. Insulin resistance raises leptin levels in the plasma and this leptin is found to have a property of increasing sympathetic nervous activity. So obesity associated hypertension is contributed by leptin dependent activation of sympathetic nervous system.

OXIDATIVE STRESS AND ENDOTHELIAL DYSFUNCTION

In non diabetic humans, lipid peroxidation which is represented by plasma thiobarbituric acid and urinary prostaglandin –F2alpha were found to be positively correlated with waist circumference and BMI, showing that fat accumulation is correlated with oxidative stress[81].

Insulin resistance produces impairment in phosphatidyl inositol 3 kinase dependent signaling pathway. This causes an imbalance between nitric oxide production and endothelin 1 secretion. This imbalance finally leads

to endothelial dysfunction. Many studies have shown that endothelial dysfunction is positively correlated with insulin resistance and hypertension[82].

ACTIVATED RENIN ANGIOTENSIN SYSTEM

By affecting function of kidney and by modulating tone of blood vessels, blood pressure is crucially regulated by rennin angiotensin system. In obese individuals' expression of certain genes like angiotensinogen, angiotensin converting enzyme is more in adipose tissue.

So there is overproduction of angiotensin II in adipose tissue of obese patients. Plasma aldosterone level was found to be higher in obese patients. It was found that the best predictor of aldosterone levels in plasma was abdominal obesity[83].

EFFECT OF OBESITY ON CIRCULATION

Obesity, by increasing the weight of the body, increases energy expenditure during physical activity which also includes moving the body. There is also an increase of basal metabolism associated with increased mass of adipose tissue. This increased energy requirements of the obese will impose a load on the circulatory system and they are not able to do the activity with as ease as the non obese persons. But it has been said that obese individuals have greater mechanical efficiency than normal subjects but there are some studies which opposes this fact. In

obesity, the blood volume per kg is reduced, but when calculated with regard to the body surface it is normal.

WEIGHT OF THE HEART IN OBESITY

Pathologists have found that hearts of obese individuals have extensive subepicardial fat depots. Another study also reported the presence of fat deposits up to 50% of the heart weight without any sign of abnormal heart function. It was said that weight of the heart increases in proportion to the body weight. Since hypertension is associated with obesity, it is possible that hypertrophy of obese heart may be due to hypertension also. In patients with obesity of long duration both ventricles are hypertrophied, but the left ventricle is mostly affected.

DIETARY LIPIDS:

The major constituents of dietary lipids are chiefly long chain triglycerides with lesser amounts of phospholipids, cholesterol, cholesterol esters and fat soluble vitamins. The triglycerides contain both saturated fatty acids (palmitic and stearic) and unsaturated fatty acids (linoleic, linolenic, arachidonic) which are essential fatty acids and contain more than one double bond. These lipids are digested almost exclusively in the small intestine. Not all of the products of fat digestion leave the intestinal epithelium without being altered during transit in the epithelial cells. Despite the fact that intraluminal digestion of

triglycerides proceeds fairly rapidly to yield appreciable quantities of fatty acids, monoglycerides and diglycerides, analysis of lymphatic fat shows that most if not all of the fats are in the form of triglycerides. This concludes that these products of fat digestion on absorption are resynthesised to a large extent back to triglycerides in the cells of the intestinal mucosa.

Free fatty acids with 12 or less carbon atoms after digestion are absorbed into portal blood. Fatty acids with 14 or more carbon atoms are found to be absorbed through lacteals. Our diet mainly contains fatty acids with 16 to 18 carbon atoms. This implies that major route of normal intestinal absorption of lipids is through lymphatics.

LIPOPROTEINS

These are molecular complexes consisting of both lipids and proteins that provide means for lipid transport between different organs and tissues. Lipids by virtue of their immiscibility with aqueous solutions depend on protein carriers for transport within bloodstream and extracellular fluids.

STRUCTURE

These are spherical having a hydrophobic core wrapped in a hydrophilic coating. The core is made up of cholesterol esters and

triacylglycerols which because of their nonpolar nature always avoid contact with water. The hydrophilic surface contains phospholipids, free cholesterol and proteins. It interacts with water in the plasma thereby promoting solubility of lipoproteins.

Composition of plasma lipids in adults

LIPIDS	CONCENTRATION (mg/dl)
TAG	40-140
Cholesterol	150-200
Phospholipids	145-250
Free fatty acids	4-20
Total	360-680

ROLE OF MICELLES IN FAT ABSORPTION:

Micelles are formed by interaction of bile salts with cholesterol. They make the lipids soluble and transport them to brush border of intestinal mucosal cell. The micelles move down their concentration gradient to the mucosal surface. On contact with the surface, the lipid portion enters the cell probably by passive diffusion. The bile salts left behind diffuse back into the chyme and take up more monoglycerides and fatty acids and transport them to brush border. The bile salts thus perform a “ferrying function” which is very important for fat absorption.

Monoglycerides are hydrolyzed to glycerol and fatty acid during entry into the epithelial cells by the lipase present in the cell.

Long chain fatty acids containing more than 12- 14 carbon atoms are resynthesized to triglycerides in the mucosal cells. The resynthesis reduces the fatty acid content inside the cell and maintains a favorable concentration gradient for the diffusion of fatty acids and monoglcerides. The synthesis occurs in the smooth endoplasmic reticulum which contains the enzymes and cofactors necessary for the synthesis of triglycerides. Free cholesterol formed from cholesterol esters by the action of esterases in the lumen and microvilli enter the cell and are re-established.

Most of the short and medium chain fatty acids (12 or less carbon atoms) leave the mucosal cell by diffusion into the portal blood. The glycerol that is liberated by complete hydrolysis is also absorbed by diffusion and some of it travels along with FFA through portal blood. The rest of the glycerol is converted to L-glycerophosphate and used in the resynthesis of triglycerides and phospholipids in the intestinal epithelial cell.

APOLIPOPROTEIN

Protein part of lipoprotein is called apolipoprotein. The most characteristic structural feature of apolipoprotein is amphipathic helix, an alpha helix in which one side is formed by hydrophobic and the other by hydrophilic amino acid side chains.

NOMENCLATURE OF LIPOPROTEINS

Many types of lipoprotein exit each having characteristic lipid and protein compositions. Their densities are inversely related to their lipid content: the higher the lipid content, the lower the density. The various classes are 1) Chylomicrons 2) VLDL 3) LDL 4) HDL

FUNCTIONS OF LIPOPROTEINS

1. They transport the dietary fat from intestinal mucosa where it is absorbed to liver by exogenous lipid transport. It is done by chylomicrons
2. Transfer triacylglycerols (TAG) and cholesterol from liver to other tissues by endogenous lipid transport. This is by VLDL and LDL.
3. Transport cholesterol from extra hepatic tissues to liver by reverse cholesterol transport. It is by HDL.

LIPOPROETIN METABOLISM

CHYLOMICRONS

The dietary TAG is transported by chylomicrons to other tissues. As the chylomicrons pass through the capillaries of tissues they bind to lipoprotein lipase (LPL). Here TAG is hydrolyzed to FFA and monoacylglycerols which diffuse directly into tissues. Chylomicrons also deliver dietary cholesterol to liver.

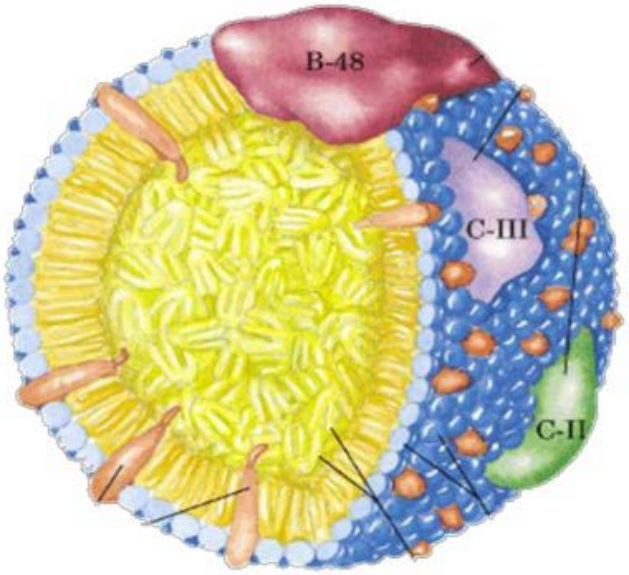
Synthesis:

Chylomicrons carry lipids of dietary origin, they are synthesized and appear in the circulation only after a meal rich in fats. Their content of cholesterol, phospholipids, fat soluble vitamins reflect the lipid composition of previous meal.

METABOLISM

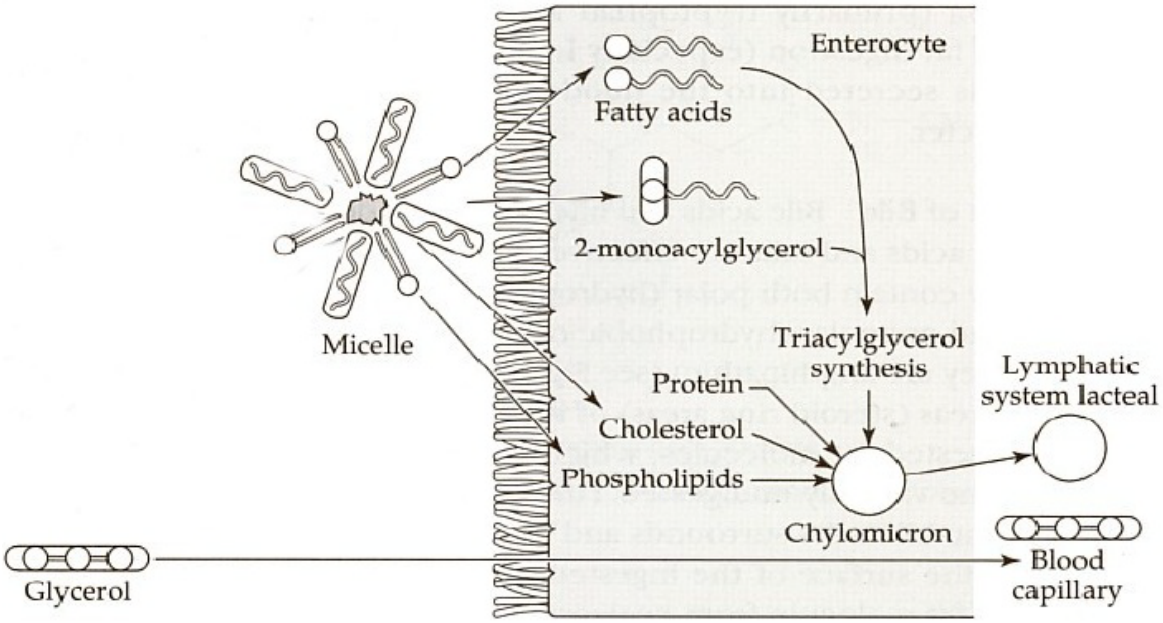
Initially they contain Apo B48 and Apo A. After entering the circulation the nascent particles acquire Apo C II and Apo E from HDL and become mature chylomicrons. It becomes functionally competent. Apo CII allows the mature particles to activate the enzyme lipoprotein lipase (LPL). The activity of LPL is under the influence of various hormones like insulin and cortisol[84]**.** Insulin causes inhibition of lipolysis, peripheral glucose uptake and stimulation of adipocyte differentiation

Structure of Chylomicron



- *Size:* 0.1–1 µm
- *Average composition*
  - TG (84%)
  - Cholesterol(2%)
  - Ester Cholesterol (4%)
  - Phospholipid (8%)
  - Apo lipoproteins (2%)

Lipid Absorption



thereby promoting triglyceride storage in adipocytes. Obesity promoting effect of cortisol has a synergistic effect with insulin by causing induction of LPL in adipose tissue. Other factors which inhibit LPL activity are testosterone, growth hormone, tumour necrosis factor (TNF) and catecholamine.

In the peripheral tissues, the activated LPL causes hydrolysis of 80-90% of chylomicron triacylglycerols. This process causes transfer of A and C apolipoproteins to HDL. These changes lead to formation of chylomicron remnants, a smaller particle. The fatty acids released from hydrolyzed triacylglycerols enter muscle and adipose tissue cells and the glycerol part enters the liver where it is used for the synthesis of TAG.

VERY LOW DENSITY LIPOPROTEIN

SYNTHESIS AND SECRETION:

Synthesis of nascent VLDL particles occurs in the hepatocytes by a series of reactions similar to chylomicrons. It involves assembly of TAG, phospholipids, cholesterol and Apo B-100.

Metabolism

Mature VLDL is acted upon by LPL in capillaries of peripheral tissues. The enzyme is activated by Apo C II of mature VLDL. The VLDL, TAG are hydrolyzed more slowly compared to those in chylomicrons with residence time in blood of 15-20minutes.

Progressive stripping of TAG is accompanied by transfer of Apo C to HDL. VLDL remnants possess Apo E which would mediate their uptake in liver. The fatty acids released from the degraded TAG are taken up mainly by peripheral tissues.

LOW DENSITY LIPOPROTEINS:

Most of the LDL is derived from VLDL and IDL but a smaller amount is released from the intestine. During its formation from VLDL, Apo B100 is the only apolipoprotein retained. Most of the TAG are lost during this transition, so that relatively higher concentration of cholesterol and cholesterol esters. Apo B100 serves a ligand for LDL receptors.

The major type of lipoprotein involved in the development of cardiovascular diseases and also the reason for insulin resistance is small dense LDL lipoproteins [85].

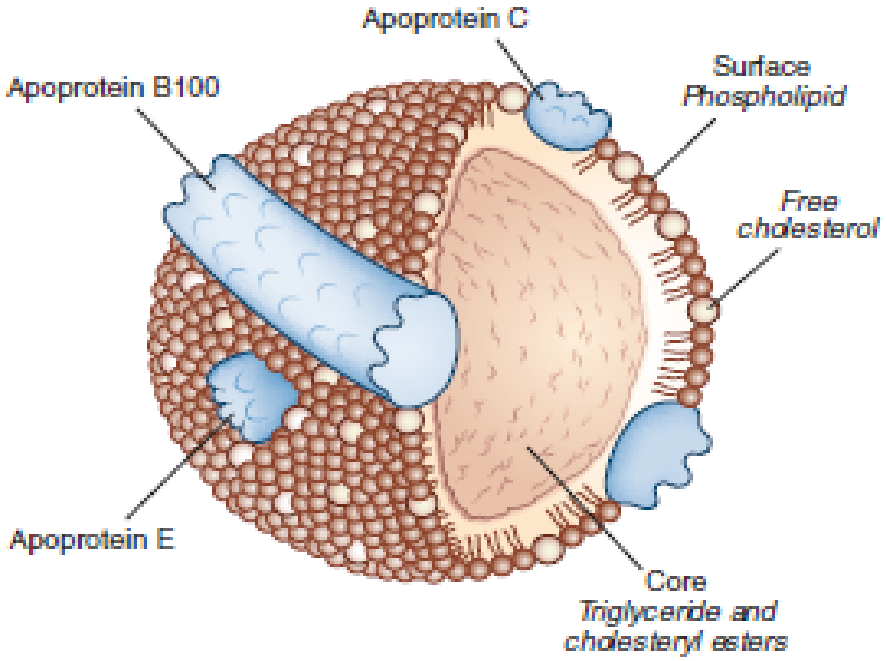


Figure 37-7 General structure of lipoproteins: schematic representation of a very-low-density lipoprotein (VLDL) particle.

LDL receptors

These receptors are present in all cells but are most abundant on hepatocytes and adrenal cortex. Helped by Apo B 100 these receptors mediate the uptake of cholesterol rich LDL molecules either by liver or peripheral tissues especially fibroblast, vascular smooth muscle, lymphocytes. It is a highly regulated process of receptor mediated endocytosis occurring via clathrin coated pits. LDL receptor is sometimes referred to as Apo B100/Apo E receptor because it has high affinity for Apo E also and can mediate uptake of IDL particles as well. It is important for whole body cholesterol homeostasis. The subsequent degradation of LDL in the lysosomal compartment of cells results in the release of cholesterol. The free receptor can then return to the surface of the cell. It will be used again for uptake of other molecules of LDL.

HIGH DENSITY LIPOPROTEINS

HDL particles are called good cholesterol because it acts as scavengers by removing free cholesterol particles from extra hepatic tissues and are then excreted through bile. They are produced by hepatocytes and intestine or being produced during the process of metabolism of other lipoproteins.

FUNCTIONS

It is involved in reverse cholesterol transport.

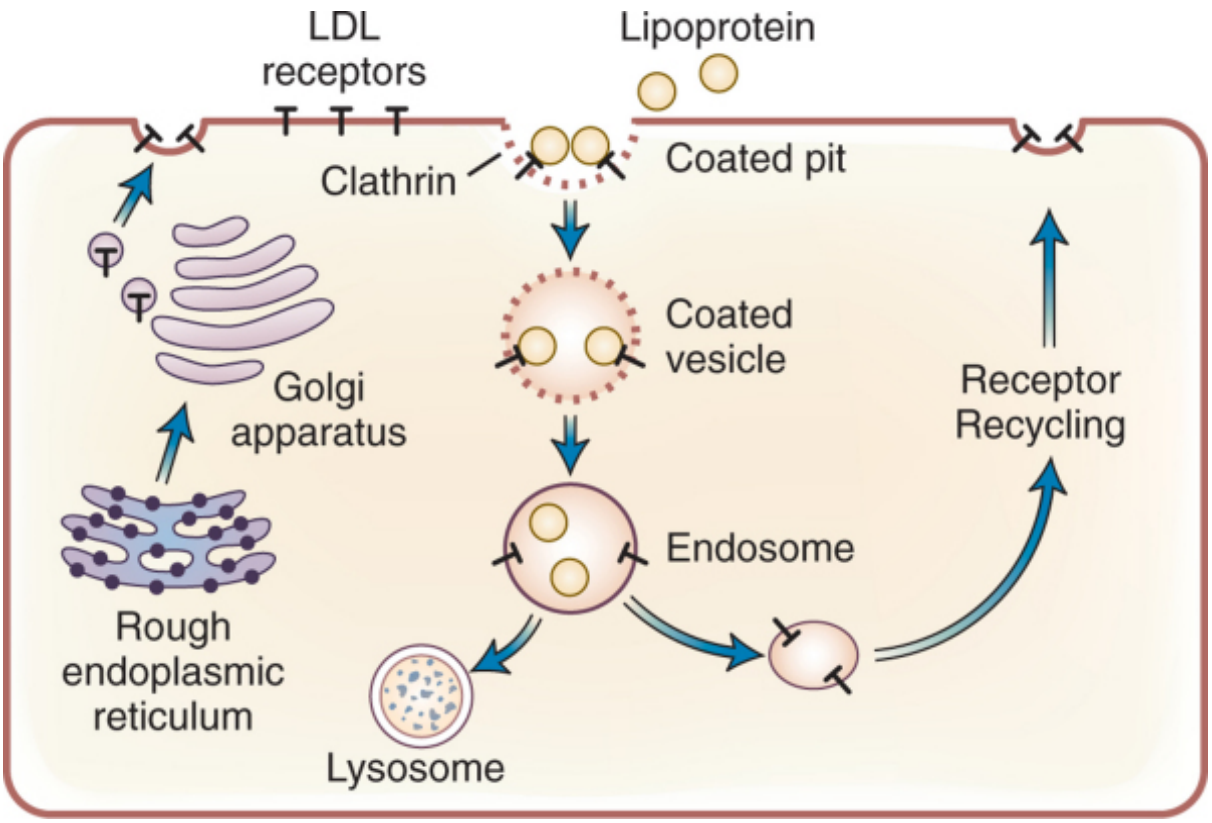
It functions as a reservoir of apolipoproteins transferring apo E and apo C to nascent chylomicrons and VLDL.

LDL and Cardiovascular risk

The initial step in formation of atherosclerosis is arterial intima being invaded by plasma LDL. The rate of LDL infiltration depends on (1) LDL level in the blood (2) arterial wall permeability[86]**.** By some process they reach the vascular sub endothelium. A part of LDL gets entrapped in extracellular matrix. This entrapped LDL is ripe for modification. Some kinds of modifications are fusion of lipoproteins, proteolysis, and aggregation. Once this modification has occurred LDL has got the capability of potential for inflammation. There will be activation of endothelial cells, smooth muscle cells and monocytes/ macrophages. In atherogenesis, the key factor is macrophages[87] **.**The macrophages undergo apoptosis and releases their excess lipid contents into the lipid pool. They also release metalloproteinases which are involved in degrading extracellular matrix destruction. All these changes produce unstable plaques which are prone to rupture.

FAT ACCUMULATION

In areas where adipose tissue is more labile, namely those areas which are depleted by starvation or expanded by hyperphagia and lipid accumulation – insulin sensitivity appears most prominent. A study by **Favarger et al** has shown clearly that the primary site of conversion of carbohydrate to fat in vivo is the adipose tissue itself[88] **.**The sensitivity of adipose tissue to insulin has permitted its use as an assay to determine minute amounts of insulin which is biologically active[89]**.**


LDL
receptors
Lipoprotein
Clathrin
Coated pit
Coated
vesicle
Golgi
apparatus
Receptor
Recycling
Endosome
Rough
endoplasmic
reticulum
Lysosome

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY DESIGN: This was a cross-sectional type of study.

STUDY CENTRE AND PERIOD: This study was carried out in Tirunelveli Medical College Hospital from August 2016 to June 2017

SAMPLE SIZE: The sample size was 100

STUDY GROUP: The study group was divided into cases and controls based on their WC and BMI values. If both the values were normal they were considered as controls. The remaining subjects with either increased WC or with increased BMI or both were taken as cases. Their parameters were analysed.

ETHICAL CONSIDERATIONS:

Institutional ethical committee clearance was obtained prior to the commencement of the study. The patients who were attending the non-communicable disease OPD were recruited for this study. All the subjects were clearly explained about the study in their own language. Informed consent was obtained from those who were willing to participate in this study.

INCLUSION CRITERIA:

- Female patients
- Age group of 20-45 years

EXCLUSION CRITERIA:

- Known diabetic and hypertensive patients
- Cardiovascular disorders,
- Thyroid disorders and
- History of Chronic steroid therapy
- Menopausal women

METHODOLOGY:

After getting informed consent, the information about past history, menstrual history was noted in a separate proforma sheet. Then General and systemic examination was done. Their anthropometric measurements like height, weight and WC were taken.

Measurement of Height:

With participants in bare feet, using a non stretchable measuring tape which was secured to the wall, height was measured in centimetres to the top of the head (nearest 0.5cm)

Measurement of weight: Using a professional body weight scale, weight was measured in kilograms, with only light clothing and after asking them to empty all belongings.

MEASUREMENT OF HEIGHT

MEASUREMENT OF WEIGHT

Measurement of BMI:

BMI was calculated using Quetlet's formula: weight (kg)/ height (m^2).

BMI(kg/m2)	Classification
18.5-22.9	Normal
23.0-24.9	Overweight
≥25	Obese

Measurement of Waist Circumference:

According to WHO STEPS protocol for measuring waist circumference, it is advisable to make measurement at the level of midpoint between lower margin of last palpable rib and top of iliac crest at the end of normal expiration. Because at this point the lungs are at their functional residual capacity and it was measured in centimetres[90].

By WC, the value more than 80cm were defined as obese and those with WC<80cm were said to be normal. The accuracy of these measurements depends on the correct positioning; the tape should be kept parallel to the floor at the level of measurement and the tightness of the measuring tape. The WHO STEPS protocol states that both for measurement of HC and WC, the tape should be snug around the body but it should not be kept so tight to cause constriction. It also recommends the use of a stretch resistant tape that provides a constant 100g tension[90].

MEASURING WAIST CIRCUMFERENCE

Measurement of Blood pressure:

Blood pressure was determined using standard mercury sphygmomanometer after 5 minutes of rest. BP ≥140/90 mm Hg were considered as hypertensive.

BLOOD INVESTIGATIONS

After an overnight fasting, under strict aseptic precautions, blood samples were collected from antecubital vein using 5ml disposable syringes.

Fasting blood sugar was estimated using EM360 Fully automated biochemical analyzer (LIQUIXX- Trinder's method)

Lipid profile was estimated using ACCUCARE CHOLESTEROL-SLR (Enzymatic colorimetric method)

Results were interpreted as [91]

PARAMETERS	**NORMALVALUES(mg/dl)**	**ABNORMAL(mg/dl)**
FBS	<126	≥126
Triglyceride	≤150	>150
T.Cholesterol	<200	≥200
LDL	≤130	>130
HDL	>50	<50

MEASURING BLOOD PRESSURE

TAKING BLOOD SAMPLE

EM 360 FULLY AUTOMATED BIOCHEMICAL ANALYSER

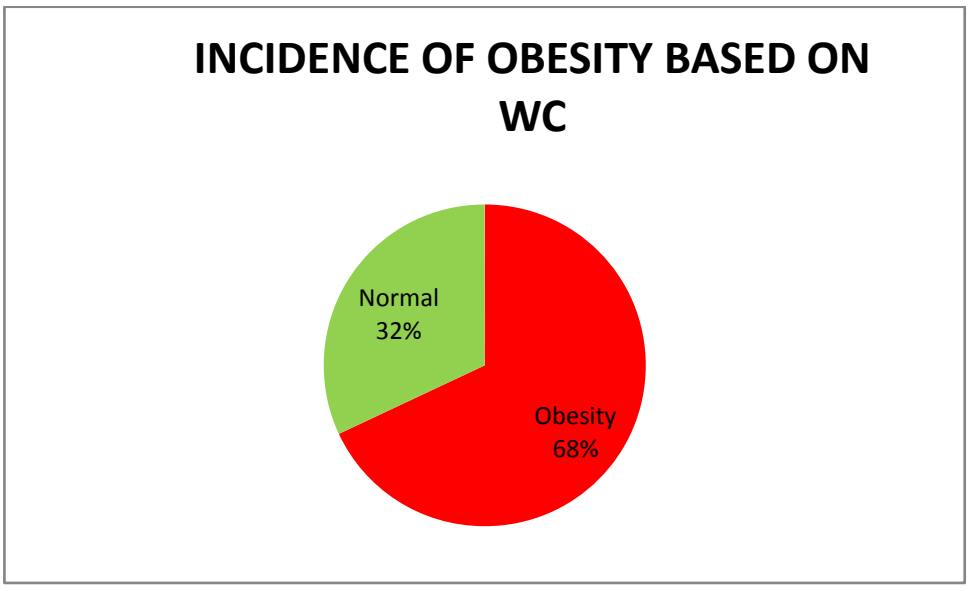
STATISTICAL ANALYSIS

STATISTICAL ANALYSIS

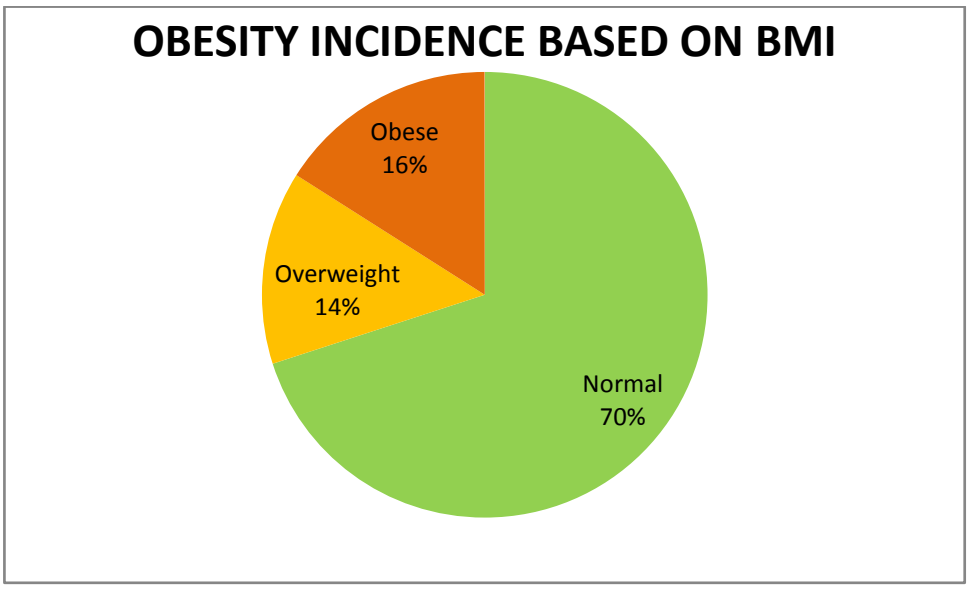
Databases like height, weight, BMI, WC and the laboratory parameters like FBS, Total Cholesterol, HDL,TGL,LDL and the blood pressure values were entered in Microsoft Excel sheet and a master chart was prepared. Statistical analysis was done by SPSS software version 20.0.

Unpaired 'T' test was used to compare the mean, standard deviation between the groups created. 'p' value less than 0.05 was taken as statistically significant. Pearson Correlation was used to evaluate the correlation coefficient.

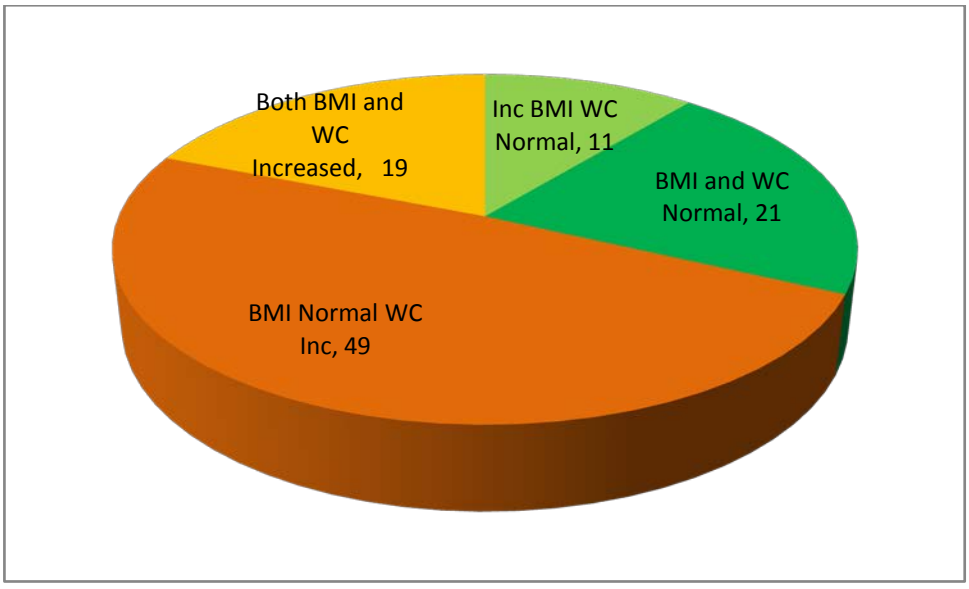
INCIDENCE OF OBESITY AMONG THE SAMPLE POPULATION BASED ON WAIST CIRCUMFERENCE



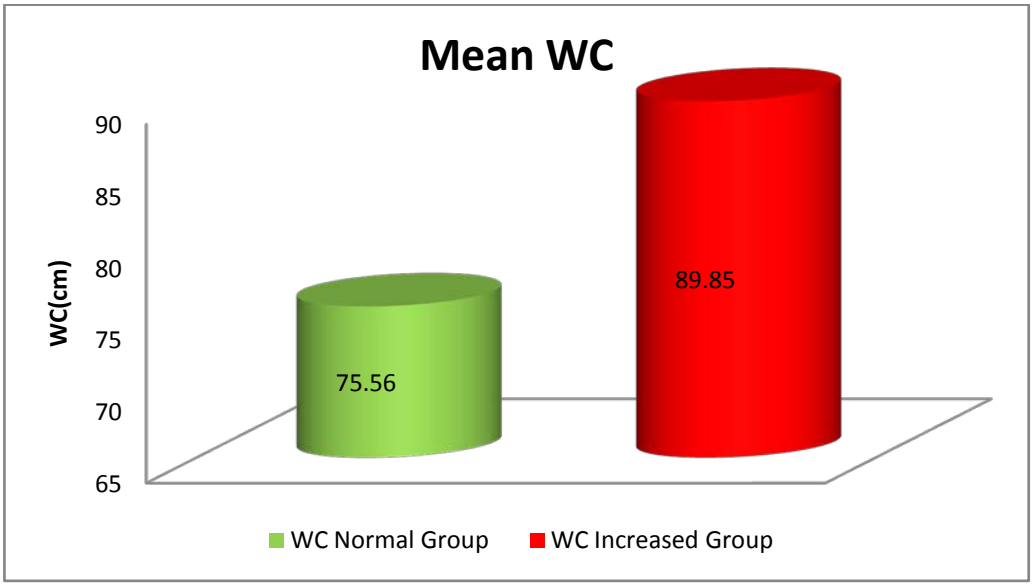
INCIDENCE OF OVERWEIGHT AND OBESITY AMONG SAMPLE POPULATION BASED ON BMI



DISTRIBUTION OF WC AND BMI AMONG SAMPLE POPULATION



MEAN WC OF THE SAMPLE POPULATION



MEAN BMI OF THE SAMPLE POPULATION

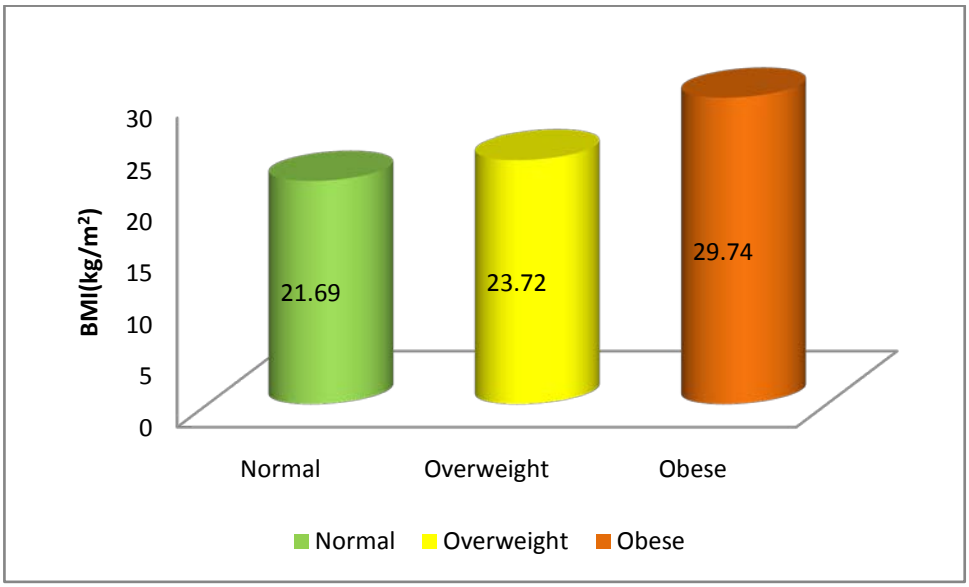


TABLE 1: ASSOCIATION BETWEEN WC AND FBS

GROUP	FBS		p Value
	MEAN	SD	
WC- Normal	98.81	22.20	<0.0001*
WC- Increased	124.97	22.02	

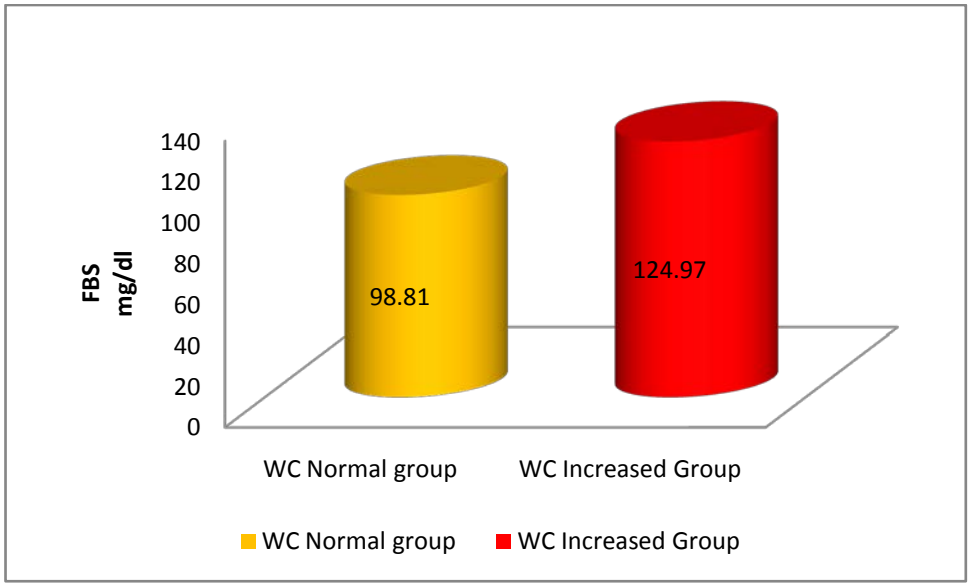
***Highly significant**

- **Highly significant association** between WC and FBS.
- FBS is significantly increased in WC increased group.

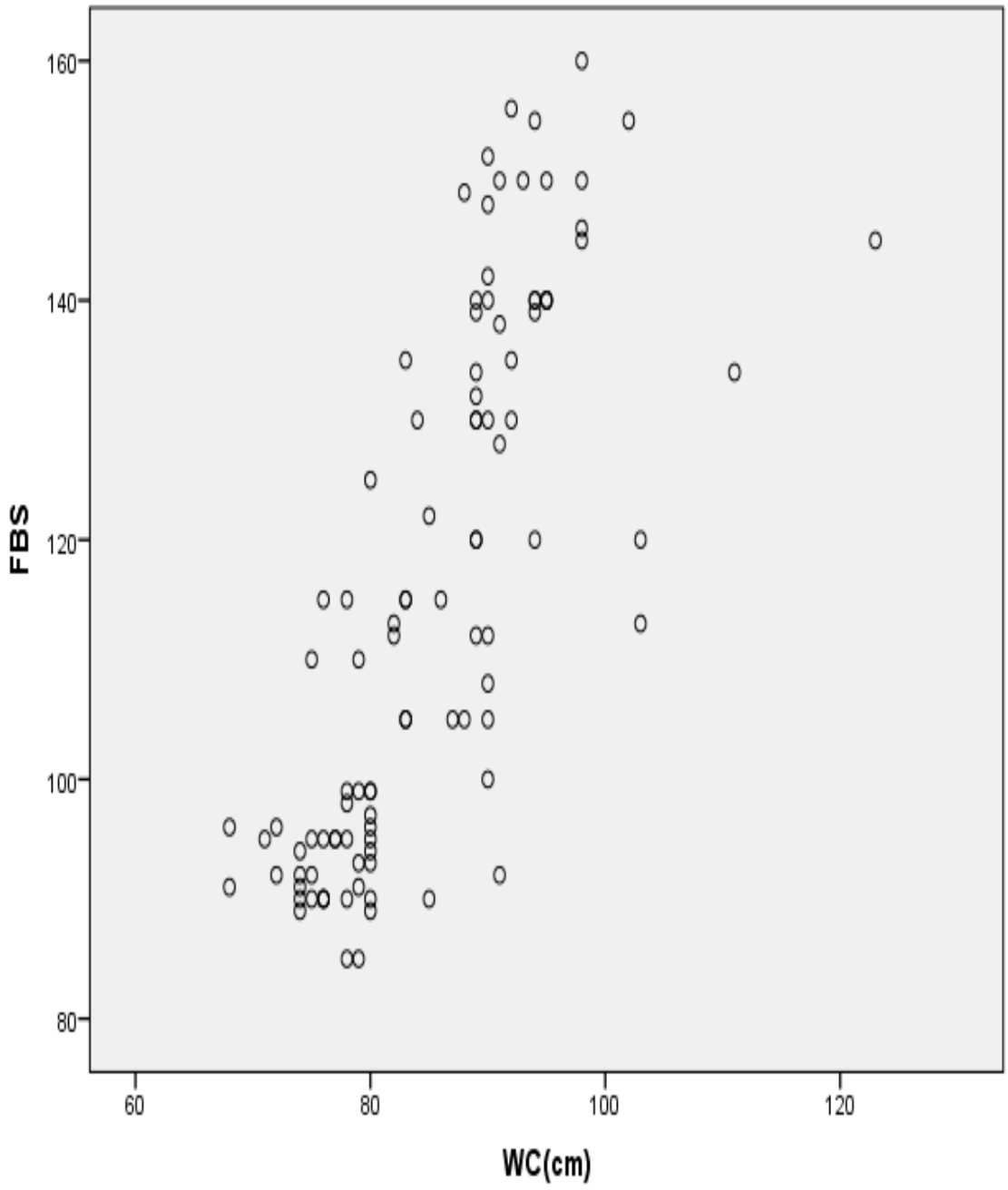
	Pearson Correlation	'p'value
WC	0.754	0.0001*

***Highly Significant**

MEAN FBS



SCATTER DIAGRAM



WC is positively correlated with FBS

TABLE 2: ASSOCIATION BETWEEN WC AND TOTAL CHOLESTEROL

GROUP	TOTAL CHOLESTEROL		p Value
	MEAN	SD	
WC- Normal	182.57	41.91	<0.0001*
WC- Increased	231.36	41.71	

***Highly significant**

- **Highly significant association** between WC and Total Cholesterol.
  - Total Cholesterol is elevated in WC increased group.

	Pearson Correlation	'p'value
WC	0.681	0.0001*

***Highly Significant**

MEAN TOTAL CHOLESTEROL

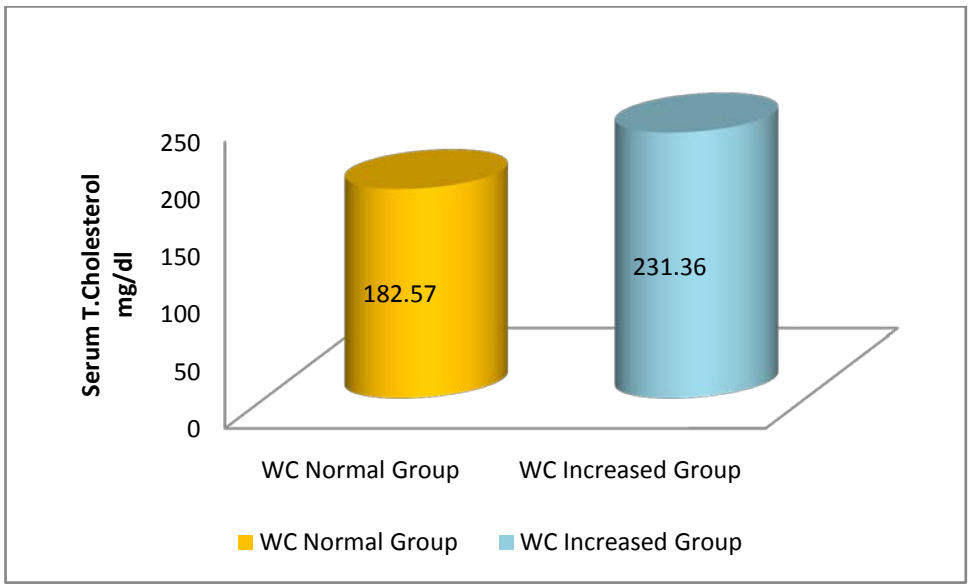


TABLE 3: ASSOCIATION BETWEEN WC AND TGL

GROUP	TGL		p Value
	MEAN	SD	
WC- Normal	138.68	21.26	<0.0001*
WC- Increased	163.05	21.22	

***Highly significant**

- **Highly significant association** between WC and TGL.
- TGL level is significantly elevated in WC increased group.

	Pearson Correlation	'p'value
WC	0.674	0.0001*

***Highly Significant**

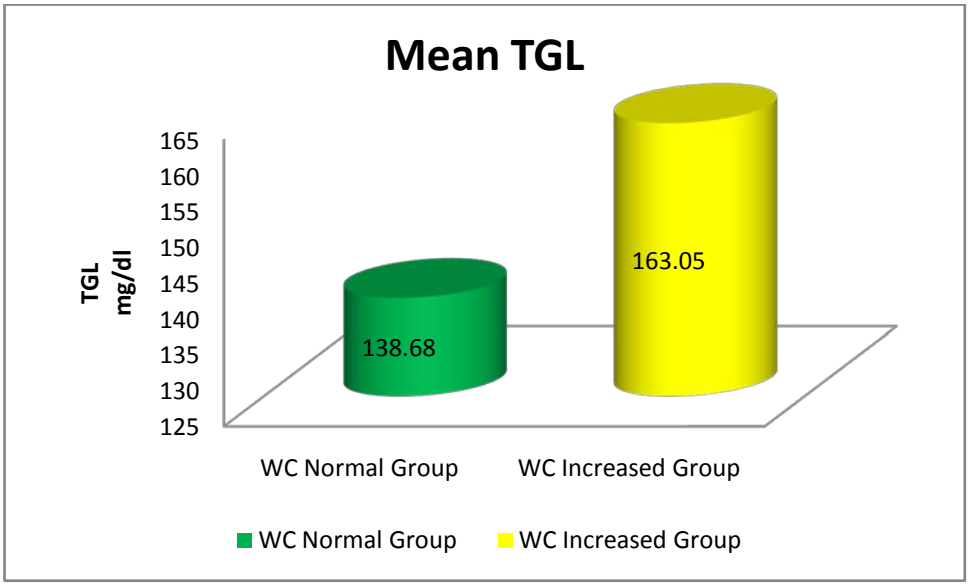


Table 4: ASSOCIATION BETWEEN WC AND HDL

GROUP	HDL		p Value
	MEAN	SD	
WC- Normal	51.12	7.19	0.0059*
WC- Increased	46.82	7.09	

***Highly significant**

- **Highly significant association** between WC and HDL.
- HDL level is significantly lowered in WC increased group.

	Pearson Correlation	'p'value
WC	-0.696	0.0001*

***Highly Significant**

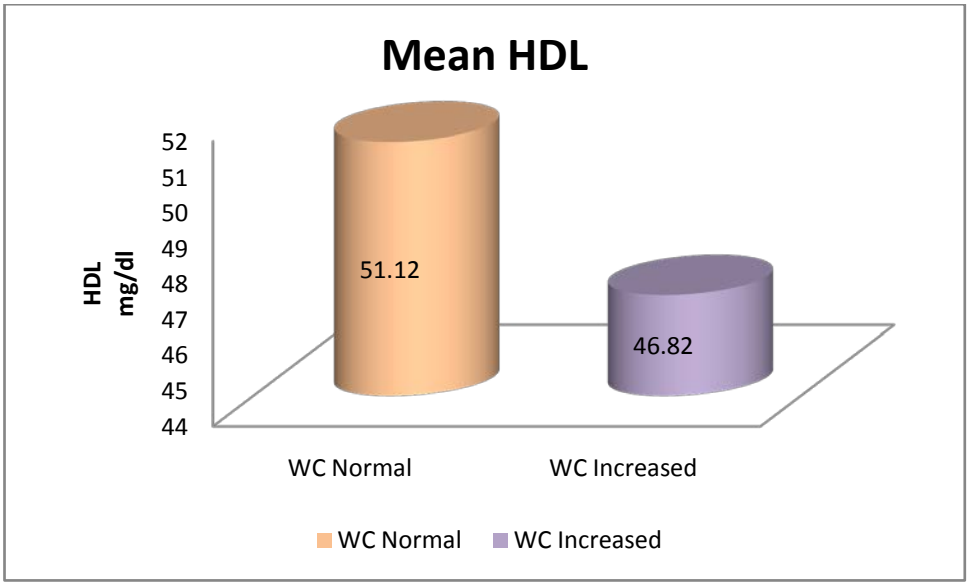


TABLE 5: ASSOCIATION BETWEEN WC AND LDL

GROUP	LDL		p Value
	MEAN	SD	
WC- Normal	103.87	46.10	<0.0001*
WC- Increased	158.47	45.475	

***Highly significant**

- **Highly significant association** between WC and LDL.
- LDL level is significantly elevated in WC increased group.

	Pearson Correlation	'p'value
WC	0.696	0.0001*

***Highly Significant**

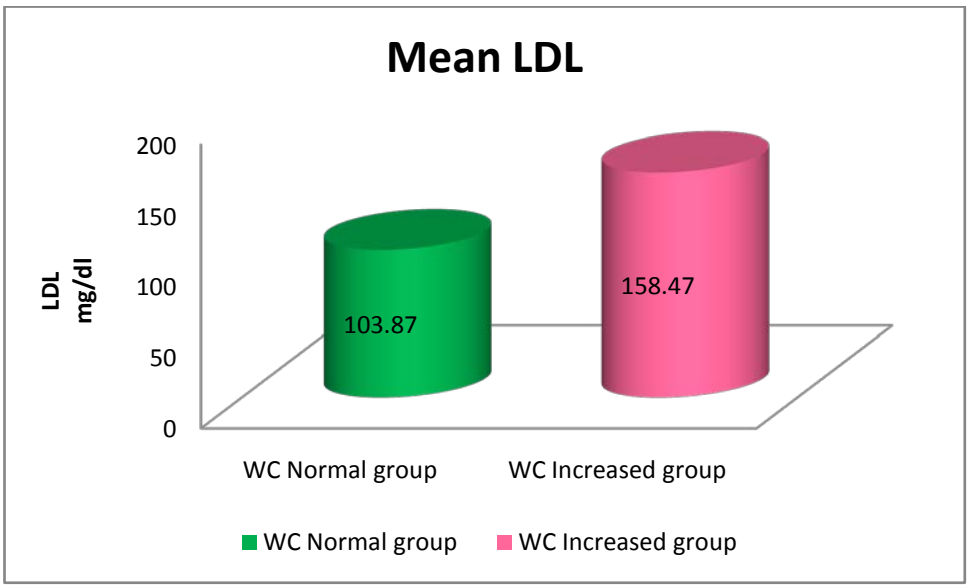


TABLE 6: ASSOCIATION BETWEEN WC AND SYSTOLIC BP

GROUP	SYSTOLIC BP		p Value
	MEAN	SD	
WC- Normal	120.37	15.88	0.0002*
WC- Increased	133.82	16	

***Highly significant**

- **Highly significant association** between WC and Systolic Blood pressure.
- Systolic BP is significantly elevated in WC increased group.

	Pearson Correlation	'p'value
WC	0.678	0.0001*

***Highly Significant**

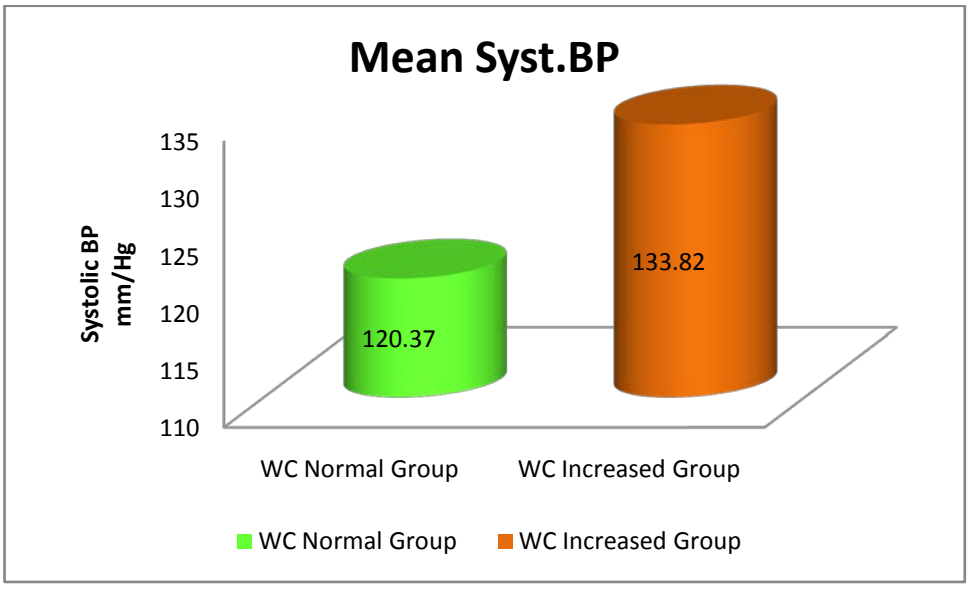


Table 7: ASSOCIATION BETWEEN WC AND DIASTOLIC BP

GROUP	DIASTOLIC BP		p Value
	MEAN	SD	
WC- Normal	75	8.63	**0.0001***
WC- Increased	82.52	8.66	

***Highly significant**

- **Highly significant association** between WC and diastolic blood pressure.
- Diastolic BP is significantly elevated in WC increased group.

	Pearson Correlation	'p'value
WC	0.423	0.0001*

***Highly Significant**

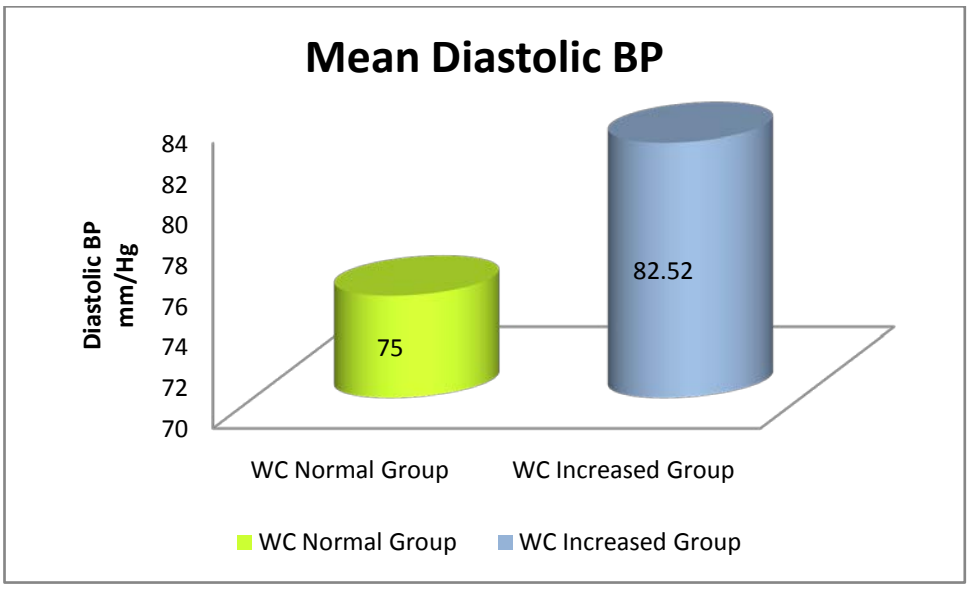


TABLE 8: ASSOCIATION BETWEEN BMI AND FBS

GROUP	FBS		p Value
	MEAN	**SD**	
BMI- Normal	116.31	21.87	**0.84**
BMI- Increased	117.26	22.00	

- p value is not statistically significant.
- BMI is not significantly associated with FBS.

	Pearson Correlation	'p'value
BMI	0.231	0.21

p value is not statistically significant

TABLE 9: ASSOCIATION BETWEEN BMI AND T.Cholesterol, TGL

GROUP	T.CHOLESTEROL		p Value	TGL		p value
	MEAN	**SD**		**MEAN**	**SD**	
BMI-Normal	210	41.78	**0.052**	153	21.18	**0.136**
BMI-Increased	**227.9**	**41.92**		**159.96**	**21.31**	

- p value is not statistically significant.
- BMI is not significantly associated with T.cholesterol and TGL.

BMI	Pearson Correlation	'p' value
T.Cholesterol	0.302	**0.002***
TGL	0.313	**0.002***

***Significant**

TABLE 10: ASSOCIATION BETWEEN BMI AND HDL

GROUP	HDL		p Value	LDL		p value
	MEAN	**SD**		**MEAN**	**SD**	**0.056**
BMI-Normal	50.7	7.12	**0.0001***	135	45.61	
BMI-Increased	42.36	7.10		154.23	45.58	

*p value is highly significant

- There is **highly significant association** between BMI and HDL.
- HDL level is significantly lowered in BMI increased group.
- BMI is not significantly associated with LDL.

BMI	Pearson Correlation	'p'value
HDL	-0.312	0.002*
LDL	0.309	0.002*

***Significant**

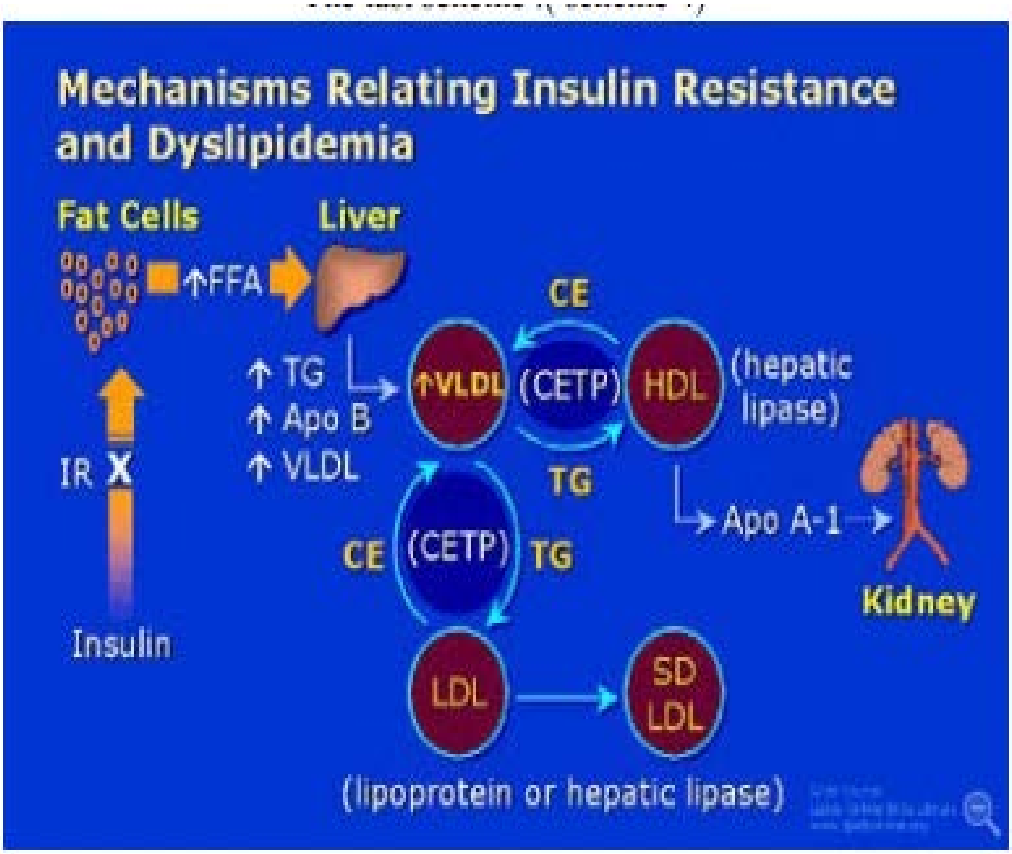
TABLE 11: ASSOCIATION BETWEEN BMI AND BP

GROUP	SYSTOLIC BP		p Value	DIASTOLIC BP		p value
	MEAN	SD		MEAN	SD	
BMI-Normal	129.17	15.79	0.73	79.37	8.65	**0.032***
BMI-Increased	130.33	15.76		83.46	8.65	

*significant

- *p value was statistically significant.
- BMI is significantly associated with diastolic BP.

BMI	Pearson Correlation	'p'value
Syst. BP	0.085	0.401
Diast.BP	0.017	0.868


Mechanisms Relating Insulin Resistance and Dyslipidemia
Fat Cells
Liver
↑FFA
↑ TG
↑ Apo B
↑ VLDL
IR X
Insulin
CE
↑VLDL
(CETP)
HDL
(hepatic lipase)
TG
Apo A-1
Kidney
CE
(CETP)
TG
LDL
SD LDL
(lipoprotein or hepatic lipase)

DISCUSSION

- Among the 100 people taken as sample, 68% of women were said to be obese based on WC as their WC value was more than 80 cm. The remaining 32% were said to be normal as their WC was less than 80 cm. Recent data from **National Family Health Survey -4** said that obesity among women is rising very fast. At present 23.6% of Indian women are obese. In the year 2005-2006 this rate was 12.6 %.
- Similarly, among the same sample population, 70% were normal as their BMI was less than 23. 14% were overweight as their BMI was between 23 and 24.99. The remaining 16% were obese as their BMI was more than 25. WHO criteria for Asian population was used to categorize sample population[92]. According to **Obesity update 2017**, women of rural areas who were less educated were two to three times more likely to be overweight and obese than educated people.
- From our study, it was found that when WC was utilized as an index for obesity more number of people was classified under the category of obesity and so medical care will be extended to more number of people. This was supported by a study by **Dalton et al**[93]. The study was carried among Australian adult population. He found

that based on BMI 20.8% of adults were classified as obese but with WC 30.5% were brought under obese category.

- In our study it was observed that 49% of the people had normal BMI but increased WC; 21% of the people had both normal BMI and normal WC; 19% of the sample population had both increased BMI and WC; the remaining 11% had increased BMI with normal WC. This revealed that greater number of people in the sample population had a normal BMI but with increased WC.
- The mean WC among the Group I (WC normal group) was 75.56 and the mean WC among Group II (WC increased group) was 89.85.

Misra and Vikram et al[94], performed a study in India to detect the validity of WC cut off values which was proposed internationally and to create action levels for Asian Indians. They declared that women with WC $\geq$ 72 cm should be considered at action level 1. This means they should be advised to lose weight or avoid increase in weight. Women with WC $\geq$ 80 cm are at the level of action 2. For them medical management of weight reduction be instituted. In our study, most of the population exceeds action 2. It's a great threat to the society. So we should initiate an action.

- From our study, the mean BMI among the normal people (BMI 18-22.9) was 21.69. The mean BMI of the people who were overweight (BMI 23-24.99) was 23.72. The mean BMI of the obese people (BMI $\geq$ 25) was 29.74
- In our study, there was a highly statistically significant association found between WC and FBS ('p' value <0.0001). Also a highly significant positive correlation between FBS and WC was seen(r<1). The mean FBS of WC normal group was 98.81 and for the WC increased group was 124.97. It was also found that no statistically significant association exist between FBS and BMI (p <0.84).

This was supported by **Ren-Nan Feng et al[95].** They analyzed data from 5 different districts of northern china which included 8940 residents. Anthropometric measurements and laboratory values were analyzed. They depicted that visceral fat is the main source of inflammatory cytokines and free fatty acids. This will lead on to insulin resistance and dyslipidemia. Thus WC was more strongly associated with diabetes mellitus than BMI.

A study by **Hans Wahrenberg et al[96]** showed that waist circumference is a strong independent risk factor for insulin resistance. It is strong enough to replace BMI, WHR and other measures of total body

fat stores to predict the occurrence of insulin resistance. It's a simple tool to exclude insulin resistance.

Insulin is a major regulator of metabolism of adipose tissue. According to **Abate N et al** , when there is genetic defect in insulin signaling, lipolysis suppression will be impaired. Release of adiponectin will be reduced . Adiponectin favors insulin sensitivity. These persons are prone to type 2 DM and metabolic syndrome. In obese persons, macrophages will invade adipose tissue**.** Release of inflammatory cytokines will occur when there is activation of these macrophages. These cytokines causes insulin resistance.

Silke Feller et al[97], did a prospective study in Europe where they investigated the association between nutrition, lifestyle and chronic diseases, 15,491 women were involved in the study. They followed them for 8 years, among the participants 425 women developed type 2 DM. They showed that to estimate the diabetic risk, both BMI and WC should be assessed but WC was more important for predicting the diabetic risk particularly in low or normal BMI individuals.

Another study by **Rangtao et al**[98]. In this study it was found that waistline in Chinese females was highly associated with T2DM. This is because visceral fat is also an endocrine organ which secretes hormones and cytokines whereas non visceral fat will not do. These secretions are

the major factors leading to the development of DM in people with increased WC. It correlated well with another study by **Tatiana Y. Warren et al[99].** They conducted the study among 834 African American Women. They showed that a significant and independent association exists between WC and FBS.

According to a study by **Yoon KH et al**, Asian ethnicity people are more prone to get diabetes even at lower levels of obesity and younger ages and thus have the tendency to develop diabetic complications much earlier.

Ian Janssen[100] conducted a study, where 14924 participants were involved. They were grouped into categories of BMI and WC according to National Institutes of Health cut offs. It was found that women who were with low or normal weight but had a large weight circumference had a 2.74 fold increased risk for cardiovascular events.

- Similarly, when compared between the groups, more incidence of dyslipidemia was seen among the group where WC was increased. The mean Total cholesterol of the WC normal group was 182.57 whereas it was 231.36 in the other group. There was a highly statistically significant association ($p<0.0001$) and also a significant positive correlation($r<1$) between WC and Total cholesterol. Thus WC increases the risk of dyslipidemia. Also in our study, BMI also

positively correlated with Total cholesterol. But more positive correlation was between Total cholesterol and WC.

This finding was supported by a study conducted among overweight and obese adolescents. It was done by **Grober Gratz et al**[101] . They showed that WC was highly correlated with dyslipidemia.

WC is as such is a risk factor for abnormal lipid profiles. Also increased blood sugar levels can itself alter lipid profile values. This was in accordance with the study by **Pietzsch J et al**[102]. They found that persons with impaired glucose tolerance and T2DM have increased catabolism of HDL, producing a low HDL value and all other lipid parameters were elevated. The reason for this finding may be decrease in the lipoprotein lipase activity which will impair the HDL particles maturation. Normally insulin leads to stimulation of lipoprotein lipase. In case of insulin resistance, this action is blunted.

It is a well known fact that increases in cholesterol has a greater risk for CVD. From the study by **Higgins et al**[103], mortality rate predicted by waist circumference was higher than other types of anthropometric measurements.

- In our study, the mean TGL value of WC increased and normal group were found to be 163.05 and 138.68 respectively. TGL level was significantly elevated in WC increased group. TGL also

showed positive correlation with BMI but was more positively correlated with WC than with BMI. It was found that when the WC increases, HDL decreases and TGL and LDL increase.

This finding goes hand in hand with a Brazilian study by **Cercato et al**[104], which was done in Sao Paulo. They assessed 1213 adults from that Brazilian population which showed that the main altered lipid profile found in central obesity was increase in TGL and or decrease in HDL levels. Studies by **Menke A et al**[105]**, Zhu S et al**[106] reported that abdominal adiposity in adults had a stronger and consistent positive correlation with TGL and TC: HDL ratio than with general adiposity. There was a little modification in the result of **Hu et al**[107]**.** His study was done in American Indians and concluded that obesity leads to decrease in HDL levels and increase in TGL levels but central obesity were more frequently associated with not much altered lipid profile.

Another kind of thought explained by **Hunter et al**[108] **and Zamboni et al**[109]. In the study by **Zamboni et al** increase in visceral adipose tissue produces increase in serum TAG level which was independent of HDL level. According to **Hunter et al,** increase in central obesity increases TAG level in post menopausal women with not much alteration of HDL level.

According to **Tarek Faour et al**[110], in central obesity, brown adipose tissue which is metabolically more active will be present around the abdomen whereas in peripheral obesity, less metabolically active white adipose tissue exists. The brown adipocytes within the abdomen will break down into its product of TGL and free fatty acids and they also release TNF and Leptin. These are the inflammatory markers. This will drain into the liver through portal system. They also tend to reduce the sensitivity of peripheral tissues to insulin.

It was found that subcutaneous fat cannot store more amount of energy. So excess energy will over flow to intra abdominal adipose tissue (IAAT) and also to skeletal muscles and liver. This causes metabolic dysfunction of the organs like insulin resistance in liver and muscles. So, we can say that the index for fatty acids overflow is IAAT.

According to **Ravi GR et al**[111], there was a direct correlation between plasma TGL level and insulin resistance. This is because TGL may influence an early pathway of insulin action. This relation is applied vice versa also.

- The mean HDL level in WC increased and normal group were 46.82 and 51.12. Both BMI and WC were negatively correlated with HDL. This means HDL level decrease with increase in WC and BMI. But HDL was more negatively correlated with WC.

Study by **Tarek Faour et al**[110] gives the reason behind the low level of HDL level in central obesity. The metabolically active abdominal adipose tissue on its break down produce free fatty acids and TGL. These products will reach the liver due to increase in hepatic uptake and they will be converted again to TGL. Thus there is an increase in the level of TGL which will stimulate the production of VLDL and Apo B. Now a situation develops with raised VLDL level and normal amount of Cholesterylester transfer protein (CETP). This will activate the exchange between TGL of HDL and VLDL. This produces HDL molecule with more of TGL and VLDL with more of cholesterylesters. So remnants of VLDL rich in cholesterol predispose to atherosclerosis and HDL with TGL will be subjected to hydrolysis in the liver by the enzyme liver lipase. HDL will get separated from the surfactant protein and thus can be easily filtered in the kidney. Thus producing a decrease in HDL level in obesity.

This was also supported by **Nevin Sanlier et al**[112]**.** They did the study to determine the association between lipids, homocysteine levels and obesity. They found that there was a negative correlation between BMI and HDL cholesterol and positively correlated with homocysteine levels. This finding was also evidenced by **Angelo Pietrobell et al**[113]**.**

- The mean LDL level in WC normal and increased groups was 103.87 and 158.47 respectively. It showed a highly significant association with WC. LDL was more positively correlated with WC than with BMI. LDL level was significantly elevated in WC increased group.

Widely accepted reason for CVD is dyslipidemia. According to **Nambi et al**[114], high level of blood glucose in obesity can influence LDL in plasma. In the presence of high blood glucose, more LDL will get glycosylated. This glycated LDL has more affinity for LDL receptors present over macrophages. This promotes foam cell formation, proliferation of smooth muscle cells and toxicity to endothelium.

The overproduction of VLDL from the liver accompanying obesity is the crucial factor for insulin resistant and hyperinsulinemia. LDL clearance is mediated by apo B/E receptor, also called LDL receptor. LDL particles are more prone to be getting modified like glycated and oxidised. They have a smaller diameter and so they can get located in the sub endothelial space from where leukocyte ingestion, inflammation and plaque transformation occur[115]**.** These modified LDL lead to reduced clearance by its receptor and produces elevated LDL level in obese individuals[116]**.**

According to **National Cholesterol Education Project**, lowering of LDL level in moderate and high risk cases can lead to decrease in their mortality due to cardiovascular events.

The initial step in formation of atherosclerosis is arterial intima being invaded by plasma LDL. They reach the vascular sub endothelium. A part of LDL gets entrapped in extracellular matrix. This entrapped LDL is ripe for modification. Some kinds of modifications like fusion of lipoproteins, proteolysis, and aggregation will occur. Once it occurred LDL has got the capability of potential for inflammation. There will be activation of endothelial cells, smooth muscle cells and monocytes / macrophages. In atherogenesis, the key factor is macrophages. The macrophages undergo apoptosis and release their excess lipid contents into the lipid pool. They also release metalloproteinases which are involved in degrading extracellular matrix destruction. All these changes produce unstable plaques which are prone to rupture.

- In our study, the mean systolic and diastolic BP of waist circumference increased group was 133.82 and 82.52 mm Hg respectively (‘p’value < 0.0001). Both were highly significantly associated with WC. BMI also showed a weak association with diastolic BP.

This finding was supported by a study conducted in Chinese population where they followed up 10,000 Chinese people including both males and females for six years concluded that rate of abdominal obesity was increased upto 62% among females and it was increased upto 30% among men. One in 5 had developed hypertension. The people who gained weight around their belly had significant risk for high blood pressure[117].

This was also supported by **Reilly et al**[118]. Excess abdominal fat directly causes overstimulation of Renin- Angiotensin- Aldosterone system. It also acts indirectly through hyperinsulinemia to produce hypertension.

Siani A, Cappuccio et al[119] conducted a study called **Olivetti Heart study**. Total of 1079 members participated in this follow up study. The results of this study showed that central adiposity leads to hypertension irrespective of insulin resistance and body mass index. It was against the finding by **Ren-Nan Feng et al.** This study among northern Chinese population indicated that BMI had a strong association with hypertension whereas WC with T2DM.

Kaushik Bose et al[120] did a study on Bengalee male jute mill workers of Belur, West Bengal. The aim of this study was to correlate waist circumference on blood pressure. They found that centrally obese people

had a greater systolic BP, diastolic BP and mean arterial pressure than centrally non obese individuals. This finding was irrespective of age and BMI. **Gerber et al**[121] also proved the same.

- BMI assess the general weight of an individual. As the weight increases, BMI increases. This will increase the peripheral resistance and body fluid volume. Increase in peripheral resistance is because of activation of renin angiotensin system producing functional constriction of peripheral vessels, alteration of cellular membranes and structural hypertrophy[122]**.**
- Finally, from our study it was found that WC was more positively correlated with FBS, lipid profile and blood pressure than BMI.

SUMMARY

&

CONCLUSION

SUMMARY AND CONCLUSION

- Obesity is a rapidly developing health problem of the society. There are few studies are available to bring out the obesity related health risks in South Tamilnadu, particularly in Tirunelveli district this study was being done. It affects both the urban and rural.
- This study was done in Tirunelveli Medical College hospital. It was a cross sectional study. Sample size was 100. Anthropometric measures were taken and blood samples and blood pressure were analysed.
- With the rising prevalence of obesity and its associated comorbidities, we have to take an action to prevent and manage this dyslipidemic state to keep the cardiovascular risks under control.
- From our study, it was found that when WC was used as a measure of obesity, more number of people was brought under obese category. So we can extend our health care system and more number of people will be advised about health maintenance. This will create a chance to lower the incidence of cardiovascular risks of the public.
- Since WC had a stronger association with fasting blood sugar, lipid profile and blood pressure than BMI, this simple measurement

using measuring tape can predict the risk of an individual. It is a simple, cost effective, non invasive method which can be considered in routine clinical practice.

- Public should be advised to maintain a low and stable WC.

"OUR WAISTLINE IS OUR LIFELINE"

FUTURE SCOPE

- In future, this study can be extended among large number of people including both males and females to detect the BEST of anthropometric measure.
- Biochemical markers like lipoprotein lipase, homocysteine can be included to improve the efficacy of WC.
- To get more information 2hr postprandial blood sugar has to be evaluated.

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ANNEXURES

INFORMED CONSENT FORM

Study Title _____

Study Number _____

Subject's Full Name _____

Date of Birth/Age _____

Address _____

1. I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. **OR** I have been explained the nature of the study by the Investigator and had the opportunity toask questions
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care or legal rights being affected.
3. I understand that the sponsor of the clinical trial/project, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. However, I understand that my Identity will not be revealed in any information released to third parties or published.
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)
5. I agree to take part in the above study

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative: _____

Signatory's Name _____ Date _____

Signature of the Investigator _____ Date _____

Study Investigator's Name _____

Signature of the Witness _____ Date _____

Name of the Witness

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
மருத்துவ ஆய்வில் பங்கேற்பதற்கு

ஆய்வு செய்யப்படும் தலைப்பு :
பங்கு பெறுபவரின் பெயர் :
பங்கு பெறுபவரின் வயது :

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் நான் படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்	☐
2	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4	இந்த ஆய்வில் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம்.....நேதி.....

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்.....

ஆய்வாளரின் கையொப்பம் / ..... இடம் ..... தேதி.....

ஆய்வாளரின் பெயர்.....

மையம் .....

கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை

சாட்சியின் கையொப்பம் / ..... இடம் ..... தேதி .....

பெயர் மற்றும் விலாசம் .....

PROFORMA

Op No: DATE:

NAME:

AGE:

SEX:

ADDRESS:

EDUCATION/OCCUPATION:

PAST HISTORY:

H/O diabetes: Yes/No

H/O hypertension: Yes/No

H/O Cardio vascular disease: Yes/No

H/O Chronic steroid therapy: Yes/No

H/O thyroid disorder: Yes/No

MENSTRUAL HISTORY:

A) Attained menopause: Yes/No

Other Medications:

GENERAL EXAMINATION

Anaemia

Icterus

Pedal oedema

Vitals:

Pulse: Temp: Respiratory rate:

Blood pressure .....in mm Hg

Anthropometric Measurements

Height: ☐ Cm

Weight: ☐ Kg

Body Mass Index: ☐ Kg/m^2

Waist circumference: ☐ Cm

Systemic examination:

Respiratory system

Cardiovascular system

Central nervous system

Any other details of illness:

Blood investigations:

Fasting blood sugar:

Lipid profile:

A) Total cholesterol B) HDL

C) LDL: D) TGL:

CONSENT: I hereby give my volunteer consent for the above study.

Signature

MASTER CHART

S.NO	Name	Age	Sex	Ht(cm)	wt(Kg)	BMI	WC(cm)	FBS(mg/dl)	T.Chol(mg/dl)	TGL(mg/dl)	HDL(mg/dl)	LDL(mg/dl)	Sys.BP(mmHg)	Dias.Bp(mmHg)
1	Jeyalakshmi	39	F	168	65	23	95	150	250	180	45	169	140	90
2	Durachi	35	F	169	60	21	95	140	270	180	45	189	140	90
3	Seethalakshmi	30	F	144	45	21.7	85	90	170	130	55	89	150	80
4	Subbhu	45	F	165	61	22.4	92	135	245	170	54	176	140	86
5	petchiyammal	40	F	150	45	20	78	95	150	125	55	70	100	70
6	sorna	39	F	170	66	22.83	94	140	216	145	50	152	140	80
7	lilly	39	F	148	48	21.9	68	96	154	134	50	77	110	80
8	prema	35	F	167	63	22.58	91	138	260	175	35	190	140	90
9	Kavitha	40	F	177	68	22	78	128	170	130	53	91	120	80
10	Amutha	39	F	165	59	21.7	93	150	267	185	50	195	140	90
11	Thangam	32	F	148	43	20	80	95	150	125	55	70	100	70
12	Nangai	39	F	164	61	22.6	90	130	245	180	45	164	140	90
13	Selvam	35	F	168	57	20.2	90	142	260	175	55	190	140	90
14	pushpam	35	F	165	59	21.7	95	140	256	185	55	189	150	80
15	thilagavathi	31	F	150	50	22.2	80	99	210	152	50	130	110	70
16	fathima	40	F	156	66	27	79	130	180	130	35	104	140	80
17	Kamala	39	F	168	57	20.2	92	156	245	165	50	173	144	90
18	Daisy	35	F	145	44	22	80	99	170	130	53	91	120	80
19	Alageswari	37	F	169	64	22.4	90	152	260	170	51	191	140	80
20	fathima	40	F	169	65	22.7	89	139	250	185	40	173	140	70
21	Shanthi	35	F	162	60	22.8	90	148	265	180	48	194	110	80
22	leelavathi	40	F	165	70	25.7	88	149	240	175	40	165	134	90
23	lalitha	38	F	168	61	22	91	150	255	185	40	178	140	90
24	sankarammal	37	F	148	48	21.9	68	130	158	129	56	76	100	70
25	varalakshmi	36	F	145	50	23.8	79	130	210	150	50	130	110	90
26	Kamatchi	32	F	168	59	20.9	94	155	230	185	55	159	150	90
27	Esther	38	F	144	45	21.73	74	91	158	129	56	76	120	80
28	Bhramachi	31	F	148	38	18	79	85	160	137	58	74	110	70

29	samuthra	40	F	139	45	23	89	132	235	150	42	163	110	94
30	Gomathi	33	F	154	59	24.89	78	115	220	160	47	141	138	80
31	uma	30	F	151	53	23.24	80	90	230	165	43	154	110	84
32	mariyammal	38	F	140	43	21.93	79	91	158	129	56	76	120	80
33	srirengam	34	F	165	57	20.9	90	100	231	143	55	170	150	90
34	latha	38	F	153	49	20.94	74	89	142	125	60	57	110	70
35	vanitha	40	F	159	65	25.7	102	155	332	165	40	259	140	90
36	barakath	32	F	153	46	19.65	74	90	145	137	52	65	120	80
37	backiyam	35	F	158	55	22	77	95	190	145	51	110	110	70
38	Deivanai	39	F	152	52	22.51	76	115	150	130	54	70	110	70
39	senthilkumari	35	F	155	55	22.8	89	140	154	145	50	75	144	80
40	Arumugam	40	F	152	50	21.6	90	105	230	165	43	154	140	70
41	Paramasakthi	32	F	141	45	22.72	74	92	164	128	54	85	120	80
42	Mahalakshmi	36	F	152	53	22.94	80	125	150	130	54	70	110	70
43	saraswathi	40	F	155	53	22.08	75	92	220	160	47	141	120	80
44	umaselvi	39	F	156	54	22.1	88	105	255	180	50	189	140	80
45	Thangamani	38	F	158	55	22.03	90	112	265	180	51	194	150	90
46	Geetha	32	F	153	50	21.3	92	130	250	140	50	193	140	90
47	Ushanandhini	38	F	160	53	20.7	90	108	248	148	45	174	140	80
48	Chidambara Vadivu	33	F	158	52	20.8	91	92	230	171	40	155	140	80
49	Thangam	38	F	158	53	21.28	71	95	150	125	55	70	100	70
50	Murugammal	32	F	157	57	23.17	76	90	154	145	52	73	140	80
51	Selvi	40	F	162	59	22.4	84	130	235	150	40	165	130	80
52	Mariyammal	39	F	152	54	23.37	76	90	176	140	50	98	138	80
53	Poomari	32	F	142	45	22.38	75	110	158	129	56	76	120	80
54	Ulagu	37	F	148	50	22.83	78	98	210	148	51	129	110	70
55	Amirdhavalli	35	F	169	59	20.6	98	146	245	190	55	172	140	90
56	fathima	37	F	165	57	20.9	94	139	221	175	55	149	160	90

57	pottu	35	F	156	63	25.92	83	115	176	140	50	98	110	82
58	Saroja	35	F	150	49	21.77	83	135	228	160	45	151	100	70
59	Amudhakani	37	F	162	59	22.4	85	122	220	160	40	148	140	80
60	chandra	35	F	151	65	28.5	82	113	174	150	50	94	110	84
61	muthu	39	F	156	60	24.69	76	95	210	148	51	129	140	70
62	nageswari	37	F	169	61	21.3	86	115	249	180	55	180	140	80
63	selvi	38	F	157	52	21.09	89	112	225	151	55	154	140	90
64	Janaki	39	F	145	48	22.8	83	105	295	152	48	234	140	80
65	Rajeswari	38	F	160	58	22.6	83	105	240	180	48	169	140	80
66	Mallika	39	F	152	55	23.8	75	90	230	165	43	154	140	70
67	Pandiyammal	36	F	142	48	23.88	78	90	230	165	43	154	136	70
68	Anitha	30	F	163	52	34.71	103	120	290	190	33	219	140	96
69	Grace	37	F	145	66	31.42	98	145	265	180	31	198	140	94
70	Visalatchi	30	F	165	56	20.5	89	130	235	174	52	166	140	70
71	Saroja	32	F	161	55	21.2	80	94	162	120	55	83	120	70
72	Lakshmi	35	F	152	67	29	76	90	236	154	39	166	140	70
73	Pitchammal	36	F	170	62	21.4	98	150	254	174	54	180	140	80
74	fathima	40	F	142	50	24.87	75	95	225	160	35	158	140	80
75	kanagamani	40	F	154	47	19.83	80	89	145	135	53	65	110	70
76	prema	32	F	145	48	22.87	89	134	210	170	52	124	140	70
77	vijaya	33	F	164	60	22.3	90	140	225	180	48	154	150	90
78	keeneth	34	F	145	48	22.87	72	92	164	128	54	85	120	80
79	jasmine Banu	33	F	161	90	35.85	98	160	260	220	25	191	150	90
80	Mareeswari	35	F	146	49	23	77	95	215	130	51	138	110	70
81	valli	32	F	156	93	38.27	123	145	245	170	35	176	140	100
82	Subbhulakshmi	32	F	147	48	22.22	89	120	224	158	49	143	100	70
83	anandhi	33	F	150	80	35.55	111	134	265	177	28	201	120	94
84	esakkiamal	34	F	154	53	22.3	91	128	215	155	50	134	150	90
85	Mahalakshmi	34	F	153	68	29.05	80	93	202	130	48	128	120	96

86	kanagavalli	30	F	162	60	22.8	87	105	205	148	50	125	140	90
87	isakkithai	37	F	147	41	18.98	78	85	164	128	54	85	120	80
88	Parvathi	33	F	148	53	25.6	80	97	219	140	50	141	120	80
89	selvi	26	F	151	48	21.05	74	94	215	130	51	138	110	70
90	Hameed	34	F	157	55	22.3	94	120	265	160	45	188	150	60
91	mariyammal	29	F	165	72	26.4	103	113	222	170	30	158	150	80
92	santhanathai	35	F	145	45	21.42	80	96	181	135	54	100	120	70
93	mary	39	F	156	55	22.63	72	96	181	135	54	100	110	70
94	sakthi	40	F	161	58	22.39	79	93	202	130	48	128	120	80
95	janu	37	F	162	60	22.8	89	120	250	180	45	169	140	90
96	priya	30	F	152	72	31.3	95	140	270	180	45	189	140	90
97	sabari	32	F	162	62	23.66	89	130	235	150	40	165	130	90
98	sindhuja	37	F	152	55	23.8	82	112	265	180	35	194	100	70
99	shameem	38	F	156	63	25.92	83	115	176	140	50	120	134	70
100	Sornalakshmi	39	F	174	66	21.7	94	140	216	145	52	174	144	90